



Simposio Internacional de Actualización en Ciencias Ejercicio Físico y Salud NSCA-IICEFS

Primera Edición - 2013

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Conferencistas: Juan Ramón Heredia Elvar, David García-López, Guillermo Peña García-Orea, MARZO EDIR DA SILVA GRIGOLETTO, Pedro Alcaraz, Azael J. Herrero.

Alumno: Juan Ramón Heredia Elvar. (iicefs@g-se.com)

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Low intensity blood flow restriction training: a meta-analysis

Jeremy P. Loenneke · Jacob M. Wilson ·
Pedro J. Marín · Michael C. Zourdos ·
Michael G. Bemben

Received: 23 July 2011 / Accepted: 3 September 2011
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Abstract The primary objective of this investigation was to quantitatively identify which training variables result in the greatest strength and hypertrophy outcomes with lower body low intensity training with blood flow restriction (LI-BFR). Searches were performed for published studies with certain criteria. First, the primary focus of the study must have compared the effects of low intensity endurance or resistance training alone to low intensity exercise with some form of blood flow restriction. Second, subject populations had to have similar baseline characteristics so that valid outcome measures could be made. Finally, outcome measures had to include at least one measure of muscle hypertrophy. All studies included in the analysis utilized MRI except for two which reported changes via ultrasound. The mean overall effect size (ES) for muscle strength for LI-BFR was 0.58 [95% CI: 0.40, 0.76], and 0.00 [95% CI: -0.18, 0.17] for low intensity training. The mean overall ES for muscle hypertrophy for LI-BFR training was 0.39

[95% CI: 0.35, 0.43], and -0.01 [95% CI: -0.05, 0.03] for low intensity training. Blood flow restriction resulted in significantly greater gains in strength and hypertrophy when performed with resistance training than with walking. In addition, performing LI-BFR 2–3 days per week resulted in the greatest ES compared to 4–5 days per week. Significant correlations were found between ES for strength development and weeks of duration, but not for muscle hypertrophy. This meta-analysis provides insight into the impact of different variables on muscular strength and hypertrophy to LI-BFR training.

Keywords KAATSU · Hypertrophy · Strength · Vascular occlusion training

Introduction

The American College of Sports Medicine (ACSM) recommends lifting a weight of at least 70% 1RM to achieve muscular hypertrophy as it is believed that anything below this intensity rarely produces substantial muscle growth (ACSM 2009). However, numerous studies using low intensity exercise combined with blood flow restriction (LI-BFR) have shown muscle hypertrophy to occur with a training intensity as low as 20% 1RM (Abe et al. 2005b, c; Madarame et al. 2008; Yasuda et al. 2010). In further support of LI-BFR, a recent review looking at potential safety issues of this type of training concluded that it offered no greater risk than traditional exercise (Loenneke et al. 2011). LI-BFR has been combined with several different types of exercise (e.g. knee extension, knee flexion, leg press, cycling, walking, elbow flexion, bench press) and most have observed significant increases in muscle hypertrophy (Abe et al. 2006, 2010a, b; Madarame et al.

Communicated by Susan A. Ward.


J. P. Loenneke (✉) · M. G. Bemben
Department of Health and Exercise Science,
The University of Oklahoma, 1401 Asp Avenue,
Room 104, Norman, OK 73019-0615, USA
e-mail: jploenneke@ou.edu

J. M. Wilson
Department of Exercise Science and Sport Studies,
University of Tampa, Tampa, FL, USA

P. J. Marín
Department of Health Sciences, European University Miguel
de Cervantes, Valladolid, Spain

M. C. Zourdos
Department of Nutrition, Food and Exercise Sciences,
The Florida State University, Tallahassee, FL, USA

Published online: 16 September 2011

 Springer

2008; Takarada et al. 2000; Yasuda et al. 2010), strength (Abe et al. 2006, 2010a, b; Madarame et al. 2008; Takarada et al. 2000; Yasuda et al. 2010), and endurance (Kacin and Strazar 2011). Interestingly, although increases in skeletal muscle hypertrophy and strength do not typically occur from an “Aerobic” mode of exercise, increased size and strength have been observed from both slow walk training (Abe et al. 2006) and cycling combined with LI-BFR (Abe et al. 2010a). Previous literature has discussed the benefits and mechanisms of blood flow restricted training in depth [for reviews please see (Loenneke and Pujol 2009; Loenneke et al. 2010; Manini and Clark 2009; Wernbom et al. 2008; Loenneke and Pujol 2011)].

Published studies hypothesize that blood flow restriction training induces skeletal muscle hypertrophy through a variety of mechanisms [for a review please see (Loenneke et al. 2010)], however, a definitive mechanism has yet to be elucidated. Proposed mechanisms include increased fiber type recruitment, metabolic accumulation, stimulation of muscle protein synthesis, and cell swelling, although it is likely that many of the aforementioned mechanisms work together.

Throughout the LI-BFR literature there exist many significant differences in study design, specifically with respect to different training variables (e.g. mode of exercise, days per week, duration, rest intervals, exercise intensity, exercise volume). Little work has been completed to identify which variables are the most important to consider when designing an optimal LI-BFR training program. A robust and quantitative approach to the problem can be provided in the form of a meta-analysis of the data. The primary objective of this investigation was to quantitatively identify which training variables result in the greatest strength and muscle hypertrophy outcomes when combining low intensity exercise with blood flow restriction.

Methods

Literature search

Searches were performed for published studies with a number of criteria. First, the primary focus of the study must have compared the effects of low intensity endurance or resistance training alone to low intensity exercise with some form of blood flow restriction. Second, to be considered for our analysis, subject populations had to have similar baseline characteristics (e.g. both untrained and trained) so that valid outcome measures could be made. Finally, the outcome measures had to include at least one measure of muscle hypertrophy as this is currently suggested to be a primary mechanism responsible for all

outcome measures of functionality (Loenneke et al. 2010). Studies reporting muscle hypertrophy as a percentage increase were excluded due to the inability to calculate an effect size. All studies included in the analysis utilized MRI except for two which reported changes in hypertrophy via ultrasound. In addition, due to the paucity of data on LI-BFR of the upper body, only studies investigating the lower body were included. Electronic databases searched included Science Citation Index, National Library of Medicine, Sport Discus, Google Scholar, and MEDLINE were searched in February 2011 back to the earliest available time that met the specifications of this meta-analysis when Abe et al. (2005c) published a foundational study on blood flow restriction training.

Exclusion of studies with irrelevant content and doublets was carried out in three steps. First, the titles of the articles were read, followed by reading of the abstracts, and finally the entire article was read. The reference lists of relevant articles were, in turn, scanned for additional articles (published or unpublished) that met the inclusion criteria. Conference abstracts and proceedings were excluded. Relevant studies were selected and searched for data necessary to compute effect size and descriptive information regarding the training protocol. Table 1 is composed of all studies meeting our meta-analysis requirements and Table 2 lists the studies excluded from analysis.

Coding of studies

Each study was read and coded by the primary investigator for descriptive information including gender and training experience. For both endurance and resistance training, we coded for frequency, mean training intensity, volume (duration of endurance and sets of strength training), and type of training split utilized. For training, frequency was coded by the number of days per week that participants trained their lower bodies. Pressure of the cuff was coded through a range dependent upon the initial and final pressure of each study. Volume for resistance and endurance training, respectively, was coded as number of repetitions performed, and average duration of the endurance training session. Because the range of repetitions was not large enough to compare within modes we compared total volume of work between all modalities. Training status was defined as untrained, recreationally active, trained, and athlete. Participants must have been performing a structured resistance-training program for at least 1 year prior to the study's onset in order to be considered as trained. In order to be considered for the athlete category, participants must have been competitive athletes at the collegiate or professional level. As described previously by Rhea et al. (2003) all studies included in the analysis were coded twice by the primary investigator to minimize coder drift.

Table 1 Studies included in the analysis

Citation	Age (years)	Gender	Training status	Exercise mode	Exercise intensity	Frequency of training	Length of training	Protocol	Measure of hypertrophy
Abe et al. (2005c)	<25	M	Rec. active	Squat and knee flexion	20% IRM	12× week	2 weeks	3 sets of 15 repetitions; 30 sec rest	MRI
Abe et al. (2005b)	<25	M	Athlete	Squat and knee flexion	20% IRM	14× week	8 days	3 sets of 15 repetitions; 30 sec rest	Ultrasound
Abe et al. (2006)	<25	M	Rec. active	Treadmill walking	50 M/Min	12× week	3 weeks	52-min walking bouts; 1 min rest	MRI
Abe et al. (2009)	<25	M	Rec. active	Treadmill walking	50 M/Min	6× week	3 weeks	52-min walking bouts; 60 sec rest	MRI
Abe et al. (2010b)	>50	M/F	Rec. active	Treadmill walking	67 M/Min	5× week	6 weeks	20 minutes walking	Ultrasound
Abe et al. (2010a)	<25	M	Rec. active	Cycling	40% VO _{2max}	3× week	8 weeks	15 minutes cycling	MRI
Beekley et al. (2005)	<25	M	Rec. Active	Treadmill walking	50 M/Min	12× week	3 weeks	52-min walking bouts; 60 sec rest	MRI
Fujita et al. (2008)	<25	M	Rec. Active	Knee extension	20% IRM	12× week	6 days	30-15-15-15 repetitions; 30 sec rest	MRI
Kacin and Strazar (2011)	<25	M	Rec. Active	Unilateral knee extension	15% MVC	4× week	4 weeks	4 sets to volitional fatigue	MRI
Madarame et al. (2008)	<25	M	Untrained	Knee extension and knee flexion	30% IRM	2× week	10 weeks	30,15,15 repetitions; 30 sec rest	MRI
Ozaki et al. (2011)	>50	M/F	Untrained	Treadmill walking	45% HRR	4× week	10 weeks	20 minutes walking	MRI

Calculation and analysis of effect size

Pre- and post-effect sizes (ES) were calculated with the following formula: [(Posttest mean – pretest mean)/pretest standard deviation]. ES were then adjusted for sample size bias (Rhea 2004; Rhea et al. 2003). This adjustment consists of applying a correction factor to adjust for a positive bias in smaller sample sizes. Descriptive statistics were calculated and univariate analysis of variance by groups was used to identify differences between training status, gender, and age with level of significance set at $P < 0.05$. When a significant F value was achieved, pairwise comparisons were performed using a Bonferroni post-hoc procedure. All calculations were made with SPSS statistical software package v.19.0 (SPSS Inc., Chicago, IL). The scale proposed by Rhea (2004) and Rhea et al. (2003) was used for interpretation of effect size magnitude. Coder drift was assessed by coding and then recoding all studies meeting our inclusion criteria. Per case agreement was determined by dividing the variables coded the same by the total number of variables (Rhea 2004; Rhea et al. 2003). The mean agreement for this analysis was 0.98.

Results

Overall ES and moderating variables are presented in Tables 3 and 4. The 48 ES for muscle strength (28 ES for LI-BFR training and 20 ES for low intensity training) and 60 ES for muscle hypertrophy (31 ES for LI-BFR training and 29 ES for low intensity training) were obtained from a total of 11 primary studies which met our criteria (Table 1).

Muscular strength

The mean overall ES for muscle strength for LI-BFR training was 0.58 [95% CI: 0.40, 0.76], and 0.00 [95% CI: -0.18, 0.17] for low intensity training (Table 1). Significant differences were found between blood flow restriction training and low intensity training ($P < 0.05$).

Moderating variables for LI-BFR training

Untrained groups gained more muscle strength than recreationally active groups, 1.38 [95% CI: 1.01, 1.76; $n = 6$] versus 0.37 [95% CI: 0.17, 0.57; $n = 21$] ($P < 0.05$), respectively (Table 3). Significant differences were found between 2–3 days per week and 4–5 day per week, 1.25 [95% CI: 0.84, 1.67; $n = 5$] versus 0.53 [95% CI: 0.21, 0.86; $n = 10$], respectively ($P < 0.05$), as well as between 4–5 days per week and 6–7 days per week, 0.53 [95% CI: 0.21, 0.86; $n = 10$] versus 0.29 [95% CI: 0.00,

Table 2 Studies excluded from the analysis

Citation	Age (years)	Gender	Training status	Exercise mode	Citation	Length Of training	Reason for exclusion
Abe et al. (2005a)	47	M	Rec. active	Knee extension		7 days	Case study
Clark et al. (2010)	<25	M/F	Untrained	Knee extension		4 weeks	Hypertrophy not measured
Cook et al. (2010)	18–50	M/F	Not reported	Knee extension		4 weeks	Training status not reported/atrophy model
Evans et al. (2010)	<25	M	Rec. Active	Heel raises		4 weeks	Hypertrophy not measured
Gualano et al. (2010)	65	M	N/A	Leg press, knee extension, squat		12 weeks	Myopathy case study
Ishii et al. (2005)	25–50	F	Untrained	Knee up, bent-knee push up, leg raise, knee flexion, squat, lunge		8 weeks	Simultaneous upper and lower body blood flow restriction
Karabulut et al. (2010)	>50	M	Untrained	Leg press, knee extension		6 weeks	Hypertrophy not measured
Karabulut et al. (2011)	>50	M	Untrained	Leg press, knee extension		6 weeks	Hypertrophy not measured
Kim et al. (2009)	<25	M	Untrained	Leg press, knee extension, knee flexion		3 weeks	Hypertrophy measured by DXA
Ohta et al. (2003)	18–52	M/F	Rec. active	Rehabilitation exercises		16 weeks	Rehabilitation from surgery
Park et al. (2010)	<25	M	Athlete	Treadmill walking		2 weeks	Hypertrophy not measured
Patterson and Ferguson (2010)	<25	F	Rec. active	Unilateral plantar flexion		4 weeks	Hypertrophy not measured
Sakuraba and Ishikawa (2009)	<25	M	Athlete	Isokinetic knee flexion/knee extension		4 weeks	Hypertrophy not measured in control group
Sata (2005)	<25	M	Rec. Active	Hip abduction, hip adduction, calf raise, squat, crunch, etc.		6 weeks	Patella tendinitis case study
Shinohara et al. (1998)	<25	M	Untrained	Isometric contractions		4 weeks	Hypertrophy not measured
Sumide et al. (2009)	<25	M	Untrained	Straight leg raise, hip joint abduction, hip joint adduction		8 weeks	Hypertrophy not measured in control group
Takarada et al. (2002)	>50	F	Untrained	Knee extension		8 weeks	Hypertrophy Reported As % Change
Takarada et al. (2004)	<25	M	Athlete	Knee extension		8 weeks	Hypertrophy reported as % change
Yasuda et al. (2005)	20–47	M	Not reported	Squat and knee flexion		2 weeks	Training status not reported

Table 3 Effect size for muscle strength

Overall	LI-BFR			Low intensity		
	Mean (95% CI)	<i>N</i> = 28	<i>P</i>	Mean (95% CI)	<i>N</i> = 20	<i>P</i>
	0.58* (0.40, 0.76)			-0.00 (-0.18, 0.17)		
Moderators						
Gender						
Male	0.58 (0.29, 0.97)	19	>0.05	0.08 (-0.03, 0.20)	11	<0.05
Female	I.D.			I.D.		
Both	0.58 (0.16, 1.01)	9		-0.20 (-0.37, -0.02)	9	
Training status						
Untrained	1.38 (1.01, 1.76)	6	<0.05	0.32 (0.13, 0.51)	6	<0.05
Recreationally active	0.37 (0.17, 0.57)	21		-0.10 (-0.20, -0.00)	21	
Athletes	I.D.			I.D.		
Days per week						
2–3	1.25 (0.84, 1.67)	6	<0.05	0.27 (0.07, 0.47)	6	<0.05
4–5	0.53 (0.21, 0.86)	10		-0.17 (-0.32, -0.14)	10	
6–7	0.29 (-0.00, 0.58)	12		-0.00 (-0.15, 0.13)	12	
Week of duration						
≤4	0.27 (0.03, 0.52)	13	<0.05	0.00 (-0.03, 0.04)	19	>0.05
5–8	0.49 (0.20, 0.79)	9		-0.05 (-0.11, 0.15)	7	
9–10	1.38 (1.02, 1.75)	6		I.D.		
Exercise mode						
Isotonic	1.08 (0.69, 1.46)	8	<0.05	0.28 (0.11, 0.44)	8	<0.05
Walking	0.42 (0.16, 0.67)	18		-0.12 (-0.23, -0.02)	18	
Cycling	I.D.			0.28 (0.11, 0.44)		
Exercise intensity						
15–30% MVC/1RM	1.08 (0.69, 1.46)	8	<0.05	0.28 (0.12, 0.44)	8*	<0.05
50–60 (m/min)	0.25 (-0.10, 0.61)	9		-0.05 (-0.20, 0.09)	9	
40–45% HRR/VO _{2max}	0.50 (0.17, 0.83)	11		-0.17 (-0.30, -0.03)	11*	
Repetitions						
60–70	1.37 (0.98, 1.76)	6	<0.05	0.32 (0.13, 0.51)	6	<0.05
Failure	I.D.			I.D.		
14–20 (min)	0.39 (0.17, 0.60)	20		-0.11 (-0.22, -0.01)	20	
Rest period (s)						
0	0.50 (0.19, 0.80)	11	<0.05	-0.17 (-0.30, -0.03)	11	<0.05
30	1.22 (0.83, 1.60)	7		0.30 (0.13, 0.47)	7	
60	0.25 (-0.08, 0.58)	9		-0.05 (-0.20, 0.09)	9	
120	I.D.			I.D.		
Cuff pressure (mmHg)						
140–220	0.50 (0.12, 0.88)	11	>0.05			
160–240	0.67 (0.35, 0.99)	16				
230	I.D.					

Overall ES and moderating variables for muscular strength. *I.D.* insufficient data (<5 ESs)

* Significant difference from low intensity training ($P < 0.05$)

0.58; $n = 12$] ($P < 0.05$), respectively (Table 3). Significant differences were found between ≤4 and 10 weeks of duration, 0.27 [95% CI: 0.03, 0.52; $n = 13$] versus 1.38 [95% CI: 1.02, 1.75; $n = 6$] ($P < 0.05$), respectively (Table 3). The isotonic exercise mode improved more

muscle strength than walking exercise mode, 1.08 [95% CI: 0.69, 1.46; $n = 8$] versus 0.42 [95% CI: 0.16, 0.67; $n = 18$] ($P < 0.05$), respectively (Table 3). Significant differences were found between exercise intensity 15–30% MVC/1RM and 50–60 m/min, 1.08 [95% CI: 0.69, 1.46;

Table 4 Effect size for muscle hypertrophy

Overall	LI-BFR			Low Intensity		
	Mean (95% CI)	<i>N</i> = 31	<i>P</i>	Mean (95% CI)	<i>N</i> = 29	<i>P</i>
	0.39* (0.35, 0.43)			-0.01 (-0.05, 0.03)		
Moderators						
Gender						
Male	0.42 (0.37, 0.47)	25	<0.05	0.00 (-0.02, 0.03)	25	
Female	I.D.			I.D.		
Both	0.26 (0.16, 0.37)	6		I.D.		
Days per week						
2–3	0.48 (0.38, 0.58)	6	<0.05	-0.00 (-0.07, 0.06)	6	>0.05
4–5	0.27 (0.18, 0.37)	7		I.D.		
6–7	0.41 (0.35, 0.47)	18		-0.00 (-0.04, 0.04)	18	
Week of duration						
≤4	0.41 (0.34, 0.47)	19	>0.05	0.00 (-0.03, 0.04)	19	>0.05
5–8	0.39 (0.29, 0.49)	9		-0.05 (-0.11, 0.01)	7	
9–10	I.D.			I.D.		
Exercise mode						
Isotonic	1.08 (0.69, 1.46)	8	<0.05	0.02 (-0.02, 0.06)	13	>0.05
Walking	0.42 (0.16, 0.67)	18		-0.05 (-0.10, -0.05)	12	
Cycling	I.D.			I.D.		
Exercise intensity						
15–30% MVC/1RM	1.08 (0.69, 1.46)	8	<0.05	0.02 (-0.02, 0.069)	13	>0.05
50–60 (m/min)	0.25 (-0.10, 0.61)	9		-0.02 (-0.08, 0.03)	8	
40–45% HRR/VO _{2max}	0.50 (0.17, 0.83)	11		-0.05 (-0.11, 0.00)	8	
Lower strength assessment						
Isokinetic	I.D.		>0.05	I.D.		>0.05
Isotonic	0.33 (0.26, 0.41)	7		-0.03 (-0.10, 0.03)	7	
Isometric	0.37 (0.30, 0.44)	7		0.00 (-0.06, 0.07)	7	
Repetitions						
60–70	I.D.		<0.05	I.D.		>0.05
Failure	I.D.			I.D.		
14–20 (min)	0.36 (0.30, 0.42)	18		-0.03 (-0.07, 0.00)	16	
45 (rep)	0.51 (0.43, 0.60)	8		0.03 (-0.01, 0.09)	8	
Rest period (s)						
0	0.37 (0.28, 0.46)	10	>0.05	-0.05 (-0.10, 0.00)	8	>0.05
30	0.44 (0.36, 0.53)	12		0.00 (-0.03, 0.05)	12	
60	0.35 (0.25, 0.45)	8		-0.02 (-0.08, 0.03)	8	
120	I.D.			I.D.		
Cuff pressure (mmHg)						
140–220	0.37 (0.28, 0.46)	10	>0.05			
160–240	0.41 (0.34, 0.44)	20				
230	I.D.					

Overall ES and moderating variables for muscular hypertrophy. *I.D.* insufficient data (<5 ESs)

* Significant difference from low intensity training ($P < 0.05$)

$n = 8$] versus 0.42 [95% CI: -0.10, 0.61; $n = 9$] ($P < 0.05$), respectively (Table 3). The total volume of work done in a workout, of about 60–70 repetitions improved more muscle strength than 14–20 min of

walking, 1.37 [95% CI: 0.98, 1.76; $n = 6$] versus 0.39 [95% CI: 0.17, 0.60; $n = 20$] ($P < 0.05$), respectively (Table 3). Significant differences were found between 0 s rest periods and 30 s rest periods, 0.50 [95% CI: 0.19, 0.80;

$n = 11$] versus 1.22 [95% CI: 0.83, 1.60; $n = 7$] ($P < 0.05$), respectively, as well as between 30 and 60 s rest periods, 1.22 [95% CI: 0.83, 1.60; $n = 7$] versus 0.25 [95% CI: -0.08, 0.58; $n = 9$] (Table 3). Correlational analysis identified significant relationships ($P < 0.01$) between ES for strength development and weeks of training duration ($r = 0.67$).

Muscular hypertrophy

The mean overall ES for muscle hypertrophy for LI-BFR training was 0.39 [95% CI: 0.35, 0.43], and -0.01 [95% CI: -0.05, 0.03] for low intensity training (Table 4). Significant differences were found between occlusion training and low intensity training ($P < 0.05$).

Moderating variables for LI-BFR training

An analysis of the differences in hypertrophy gains achieved for blood flow restriction training was performed in males as compared to combined gender groups to determine whether gender influenced hypertrophy gains. The male group gained more hypertrophy than the combined group, 0.42 [95% CI: 0.37, 0.47; $n = 25$] versus 0.26 [95% CI: 0.16, 0.37; $n = 6$] ($P < 0.05$), respectively (Table 4). Significant differences were found between 2–3 days per week and 4–5 days per week, 0.48 [95% CI: 0.38, 0.58; $n = 6$] versus 0.27 [95% CI: 0.18, 0.37; $n = 7$], respectively ($P < 0.05$). The isotonic exercise mode improved more muscle hypertrophy than the walking exercise mode, 0.44 [95% CI: 0.34, 0.47; $n = 13$] versus 0.31 [95% CI: 0.25, 0.38; $n = 14$] ($P < 0.05$), respectively (Table 4). Significant differences were found between exercise intensity 15–30% MVC/1RM and 50–60 m/min walking speed, 1.08 [95% CI: 0.69, 1.46; $n = 8$] versus 0.25 [95% CI: -0.10, 0.61; $n = 9$]. The total volume of work done in a workout with 45 repetitions improved more muscle hypertrophy than 14–20 min of walking, 0.51 [95% CI: 0.43, 0.60; $n = 8$] versus 0.36 [95% CI: 0.30, 0.42; $n = 18$] ($P < 0.05$), respectively (Table 4).

No significant relationships were found ($P > 0.05$) between ES for hypertrophy and weeks of duration.

Discussion

The findings of this meta-analysis confirm previous ACSM recommendations that regular low intensity resistance training (not to muscular failure) does not provide an adequate stimulus to produce substantial increases in strength or muscle hypertrophy. However, when that same low intensity exercise is combined with blood flow restriction, significant increases are found comparable to a

previous meta-analysis using higher intensities (HIT) (Krieger 2010) with both strength (LI-BFR 0.58 vs. HIT 0.80) and muscle hypertrophy (LI-BFR 0.39 vs. HIT 0.35). To our knowledge, this is the first meta-analysis completed on this novel mode of training, which shows the overall effect from manipulating different variables for training adaptation.

Subject characteristics

Subjects who were previously untrained have greater increases in muscular strength than those who were recreationally active. This may also provide some explanation for the lower effect size observed with strength in the LI-BFR cohort compared to a previous meta-analysis on HIT resistance training which was composed almost exclusively of untrained subjects. No such comparison could be made for hypertrophy as a result of insufficient data from available studies. No studies meeting our criteria have been completed investigating LI-BFR using only females, thus for this analysis males were compared to a combined group made up of both males and females (males vs. males/females). The combined group observed significantly less muscle hypertrophy than the male only group, possibly due to a buffering effect of females. This would be consistent with previous research demonstrating that women experience smaller changes in muscle size compared with men (Ivey et al. 2000). A comparison across age groups could not be made due to insufficient data from the studies included in this analysis.

Training frequency

The analysis found that strength and muscle hypertrophy were both significantly greater in the groups performing exercise 2–3 days per week compared to those exercising 4–5 days per week. It is possible that the gains were attenuated in the 4–5 day/week group from an overtraining response, even though the external resistance was low, however, it is more likely this overtraining response is more reflective of the frequency of training rather than the days trained per week, since 4 out of 7 studies in the 4–5 day/week group trained twice per day.

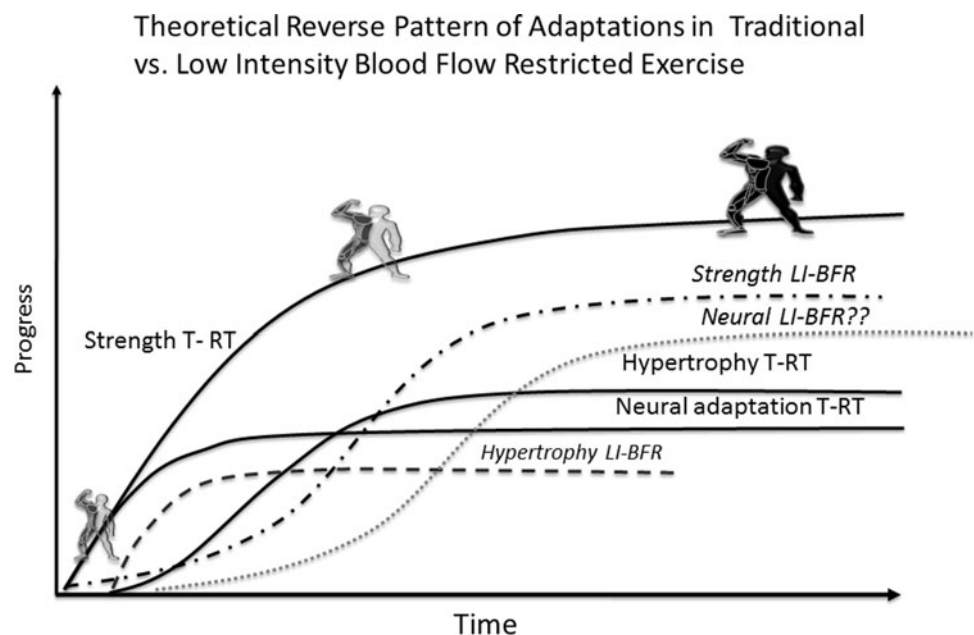
Training duration

This investigation found that although the ES for muscular hypertrophy remains fairly constant from <4 weeks of training to 10 or more weeks of training, muscular strength responds much differently. The ES indicate that muscular strength does not significantly increase until the 10 week time point (Fig. 1). This finding is interesting because traditionally it has been thought that neural adaptations

Fig. 1 The effect sizes (ES) for muscle strength and hypertrophy with low intensity blood flow restriction (LI-BFR) as it relates to duration of training



Fig. 2 Graphical representation of the theoretical interaction between strength, hypertrophy, and neural adaptations during both traditional resistance training (T-RT), and low intensity blood flow restricted exercise (LI-BFR) is shown. During T-RT strength increases at first primarily by changes in muscular hypertrophy followed later by neural adaptations. For LI-BFR the opposite pattern may occur (adapted from Sale 1988)



increase strength during the first couple of weeks of exercise and muscle hypertrophy occurs later on in the training (>6 weeks). These data suggest that perhaps the traditional training adaptation paradigm is reversed with LI-BFR exercise. This may help to explain the findings of studies which report that the strength gains from LI-BFR exercise are a product of muscle hypertrophy and not neural adaptation (Fujita et al. 2008; Takarada et al. 2002, 2000; Yasuda et al. 2011). All of those studies with the exception of one (Takarada et al. 2000) trained <8 weeks. If the findings from this analysis are accurate and representative, then it is conceivable that neural adaptations for LI-BFR exercise do not occur until much later in the training program, and studies lasting <10 weeks would be unlikely to

produce relative strength gains (maximal voluntary strength per unit muscle cross sectional area). In further support, correlational analyses found a significant relationship between the ES for strength and weeks of training, with no significant correlation found for hypertrophy. This possible reversal in the neural adaptation finding warrants further investigation before these phenomena can be definitively acknowledged. It is also possible that this finding is spurious and exclusive only to the two long-term (9–10 weeks) studies included in this analysis. While this finding is far from conclusive; however, Fig. 2 graphically depicts the possible theoretical interaction between strength, hypertrophy, and neural adaptations during both traditional resistance training, and LI-BFR exercise.

Training modality and intensity/volume

The results indicate that isotonic exercise improved muscular strength and hypertrophy to a greater degree than walking. This difference is likely related to the amount of work completed by the muscle as well as the accumulation of metabolites. With resistance training, specific muscles are easily isolated and the metabolic accumulation is much larger than that observed with walking, which further highlights the importance of metabolic accumulation for ideal outcomes in strength and hypertrophy. An additional mechanism responsible for adaptations caused by LI-BFR may be acute cell swelling as this has been shown to stimulate an anabolic response in hepatocytes (Haussinger 1996). Regardless of the mechanism, significant differences exist between isotonic resistance training and walking with LI-BFR. Therefore, individuals capable of performing low intensity resistance training with blood flow restriction will see larger increases in strength and muscle hypertrophy compared to those walking with blood flow restriction. Subsequent alterations in muscular strength and muscle hypertrophy outcomes were also significantly dependent upon exercise intensity. To illustrate, resistance training with 15–30% MVC/1RM produced greater strength and size gains compared to walking at 50–60 m/min. However, these results are likely to be an artifact of the exercise modality, which the aforementioned analysis demonstrated can impact the overall effect. Similar results are present in relation to volume of exercise and rest interval. For example, greater gains in strength and size were found; however, the only two comparisons were made between repetitions completed and minutes walked. In addition, this analysis found that 30 s of rest between sets produced much greater strength gains than 60 s; however, every study using 60 s rest was a walking study. Thus, we suggest that future investigators specifically analyze the question of volume within a given exercise modality.

Cuff pressures

Throughout the literature, numerous cuff pressures are used. Often, training studies begin at an overall low pressure and progress to high pressures throughout the training programs. For this analysis, two of our groups have overlap, but differed at where the initial training pressures began (140 vs. 160 mmHg) and where the final training pressures ended (160–240 mmHg). This overlap may have led to the non-significant finding, however it may also indicate that the absolute pressure needed for muscular adaptation is much less than commonly thought, especially when using a wider cuff to induce blood flow restriction (Crenshaw et al. 1988). In support of this, evidence suggests that higher restrictive cuff pressures (200 mmHg) are

no more effective at increasing intramuscular metabolites than moderate pressures (~150 mmHg or 130% systolic BP) when using a wide (18.5 cm) cuff (Suga et al. 2010). The impact of cuff width was not able to be made from the current analysis, since most studies in this meta-analysis used a narrow cuff (5 cm), therefore the overall impact of cuff width on training adaptation remains unknown. Current research on acute LI-BFR exercise (Wernbom et al. 2008) and the data from this analysis do not suggest that higher pressures would be more effective than lower pressures for inducing training adaptations. However, no study to date has examined the impact of progressively increasing or maintaining restrictive cuff pressure during LI-BFR training so it is not clear if progressive increases in restrictive cuff pressure are necessary to produce muscular strength or hypertrophy.

Limitations for endurance-based outcomes

The primary focus of our meta-analysis was the effects of blood flow restriction training on hypertrophy and strength training. However, it should be emphasized that our results do not necessarily apply to other outcomes such as endurance performance. For example, we found that greater training frequencies may not be ideal for hypertrophy and strength gains; however, they may be beneficial for endurance outcomes. This was illustrated by Kacin and Strazar (2011) who found that high frequency (4× week) LI-BFR resulted in small gains in hypertrophy, and no significant increases in strength. However, they found that the blood flow restricted group increased endurance performance by 63% as compared to 36% in the control condition. Moreover, while our results strongly indicate that a resistance exercise mode is ideal for strength and hypertrophy, a number of researchers have demonstrated that cycling under ischemic conditions may be a highly effective mode for increasing muscular endurance (Kaijser et al. 1990; Nygren et al. 2000; Sundberg et al. 1993). For the reason that endurance adaptations are an important, yet understudied, component of LI-BFR exercise training we suggest future research attempt to disseminate exactly what the ideal prescription is for those particular outcomes.

Conclusions

This meta-analysis provides insight into the overall impact of different training variables on muscular strength and hypertrophy to LI-BFR training. Although only 11 studies met the inclusion criteria for this meta-analysis, general recommendations can be made from the results and patterns observed from this study. This analysis provides evidence and recommendations for future studies to use in

order to maximize the muscular strength and hypertrophy response to this novel mode of training. It appears that blood flow restriction combined with low intensity resistance exercise produces a much greater response than blood flow restricted walking. Furthermore, LI-BFR training 2–3 days per week appears to maximize the training adaptation and there is some evidence that the neural adaptation to LI-BFR training does not occur at the beginning of a training program as it does with traditional resistance training. It appears that initial increases in strength may be due solely to muscle hypertrophy, while the neural impact on strength gains may occur much later with LI-BFR training. Although this finding may be true with LI-BFR training, longer-term studies are needed before a definitive conclusion can be made.

Conflict of interest The authors report no conflict of interest.

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