BLOOD FLOW RESTRICTION: Scoping Review

MICHAEL JEANFAVRE PT, DPT, OCS, CSCS

Objectives

1. Blood Flow Restriction (BFR) Defined
2. Effectiveness of BFR: local & system physiology
3. Mechanisms of BFR
4. Safety & Side Effects
5. Practical/Clinical Application

Blood Flow Restriction Defined

OBJECTIVE #1

Blood Flow Restriction – Definition & History

- training entails applying a **tourniquet-style cuff** on the proximal aspect of a limb just prior to exercise
- cuff is manually tightened or pneumatically inflated to a pressure that **occludes venous flow yet allows arterial inflow**
- originally **conceived and developed in Japan in the late 1960's** by Yoshiaki Sato and termed KAATSU training
- Prior to 2008 LL-BFR training equipment was scarce outside of Japan
- Thus far, research results regarding the efficacy of LL-BFR have been consistent and promising

Effectiveness of Blood Flow Restriction

OBJECTIVE #2

Effectiveness of Blood Flow Restriction

- exercise + blood-flow restriction (BFR) → hypertrophic adaptations with much lower exercise (<50% 1RM) intensities than previously believed[3,15,24,34,41,43,63,74-80]
- exercise protocols with tourniquet,[81] pressurized cuff,[80] or elastic banding that is applied over the proximal portion of the upper or lower extremities[43]
- Low Intensity BFR Hypertrophy = Moderate/High intensity hypertrophy [20]
  - NOT clear if muscle hypertrophy can be optimized by BFR + ↑ external loads OR if the ceiling for maximal hypertrophy is achieved with low-moderate loads[14]

Effectiveness of BFR – Muscle Adaptation

Low intensity blood flow restriction training: a meta-analysis

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

11 Included Studies

Loenneke et al. 2012[86]

Effectiveness of Blood Flow Restriction – Muscle Adaptation

Table 1 Studies included in the analysis

Citation	Age (years)	Gende	Training status	Exercise mode
Abe et al. (2005c)	<25	M	Rec. active	Squat and knee flexion
Abe et al. (2005b)	<25	M	Athlete	Squat and knee flexion
Abe et al. (2006)	<25	M	Rec. active	Treadmill walking
Abe et al. (2009)	<25	M	Rec. active	Treadmill walking
Abe et al. (2010b)	>50	M/F	Rec. active	Treadmill walking
Abe et al. (2010a)	<25	M	Rec. active	Cycling
Beekley et al. (2005)	<25	M	Rec. Active	Treadmill walking
Fujita et al. (2008)	<25	M	Rec. Active	Knee extension
Kacin and Strazar (2011)	<25	M	Rec. Active	Unilateral knee extension
Madarame et al. (2008)	<25	M	Untrained	Knee extension and knee flexion
Ozaki et al. (2011)	>50	M/F	Untrained	Treadmill walking

Loenneke et al. 2012[86]

Effectiveness of Blood Flow Restriction – Muscle Adaptation

Citation	Exercise intensity	Frequency of training	Length of training	Protocol	Measure of hypertrophy
Abe et al. (2005c)	20% 1RM	12× week	2 weeks	3 sets of 15 repetitions; 30 sec rest	MRI
Abe et al. (2005b)	20% 1RM	14× week	8 days	3 sets of 15 repetitions; 30 sec rest	Ultrasound
Abe et al. (2006)	50 M/Min	12× week	3 weeks	52-min walking bouts; 1 min rest	MRI
Abe et al. (2009)	50 M/Min	6× week	3 weeks	52-min walking bouts; 60 sec rest	MRI
Abe et al. (2010b)	67 M/Min	5× week	6 weeks	20 minutes walking	Ultrasound
Abe et al. (2010a)	40% VO_{2max}	3× week	8 weeks	15 minutes cycling	MRI
Beekley et al. (2005)	50 M/Min	12× week	3 weeks	52-min walking bouts; 60 sec rest	MRI
Fujita et al. (2008)	20% 1RM	12× week	6 days	30-15-15-15 repetitions; 30 sec rest	MRI
Kacin and Strazar (2011)	15% MVC	4× week	4 weeks	4 sets to volitional fatigue	MRI
Madarame et al. (2008)	30% 1RM	2× week	10 weeks	30,15,15 repetitions; 30 sec rest	MRI
Ozaki et al. (2011)	45% HRR	4× week	10 weeks	20 minutes walking	MRI

Loenneke et al. 2012[86]

Effectiveness of BFR – Muscle Adaptation

Low intensity blood flow restriction training: a meta-analysis

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

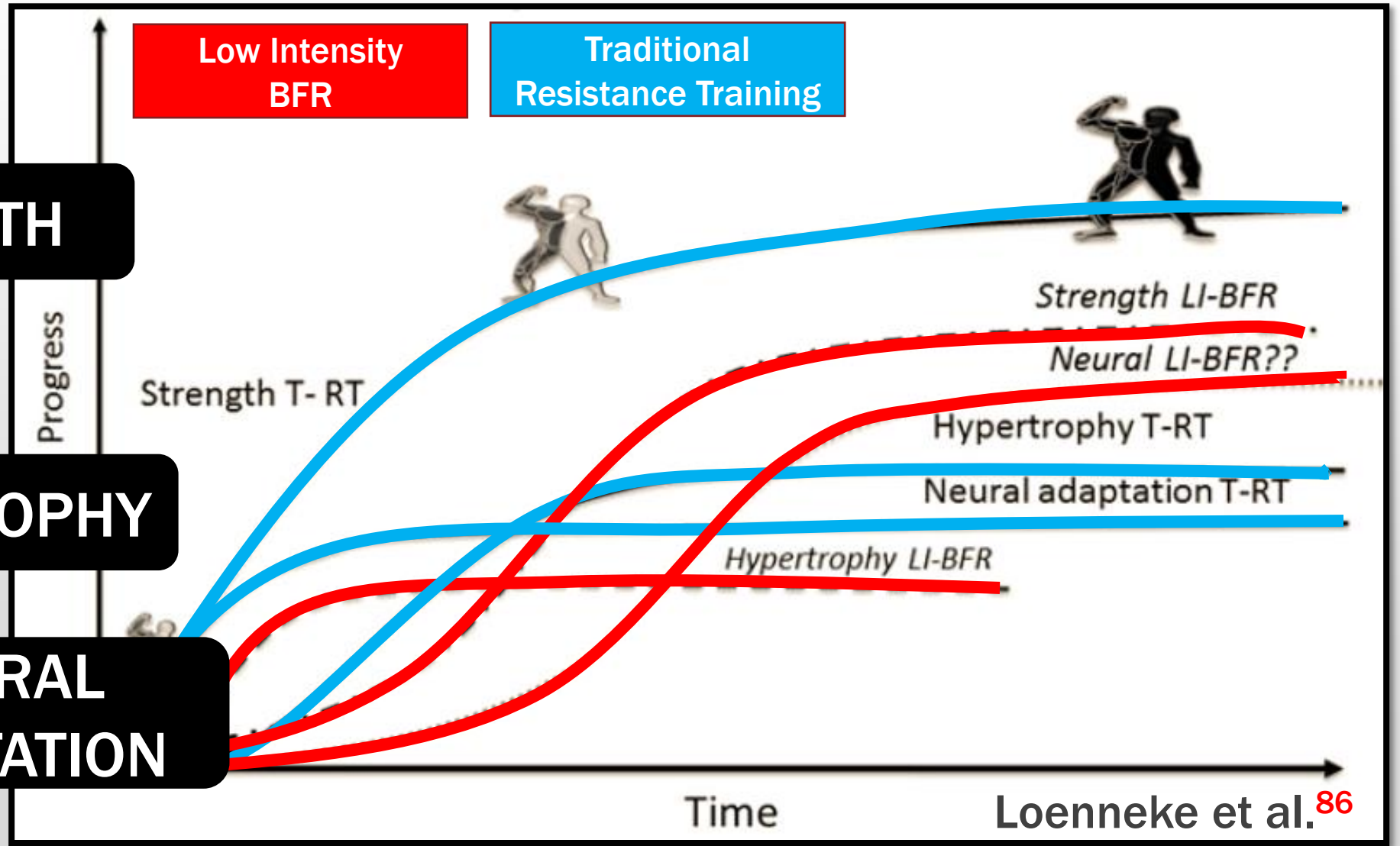
1. BFR resulted in significantly greater gains in strength and hypertrophy when performed with resistance training than with walking.

2. LI-BFR 2–3 days/week → greatest ES compared to 4–5 days/week

3. Significant correlations were found between ES for strength development & weeks of duration, but not for muscle hypertrophy

Loenneke et al. 2012

Effectiveness of Blood Flow Restriction - Timing

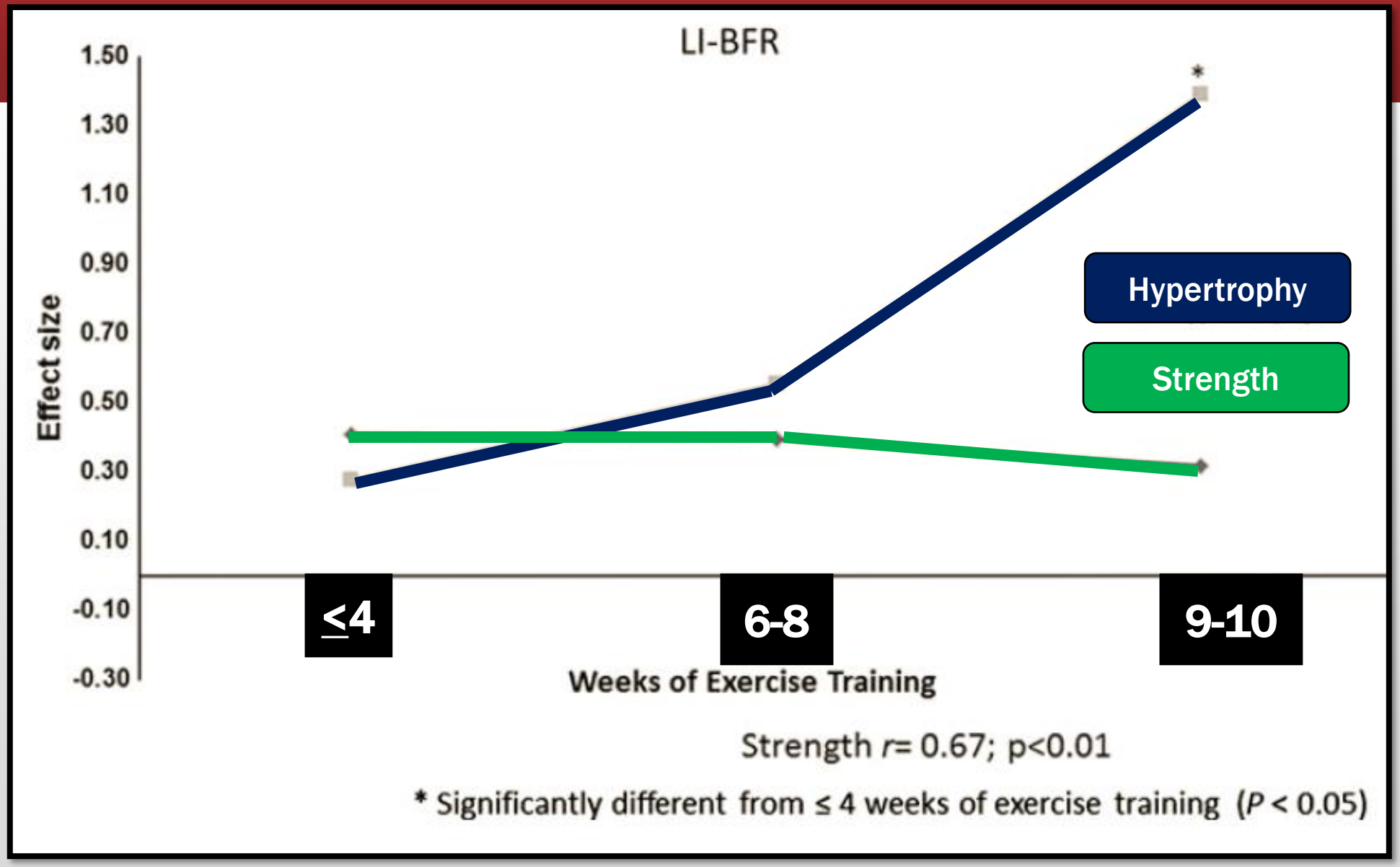


STRENGTH

HYPERTROPHY

NEURAL ADAPTATION

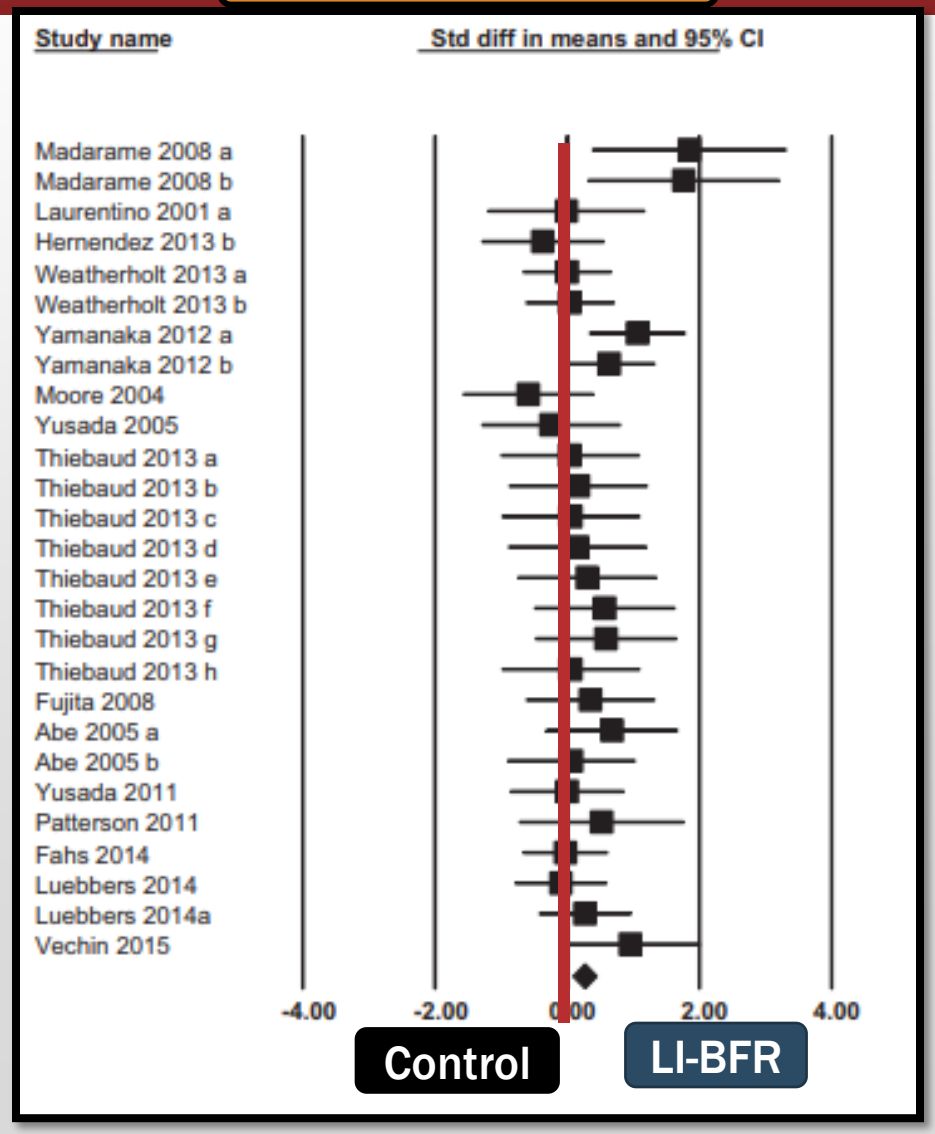
Effectiveness of Blood Flow Restriction - Timing



Loenneke et al. 2012[86]

Effectiveness of Blood Flow Restriction - Resistance

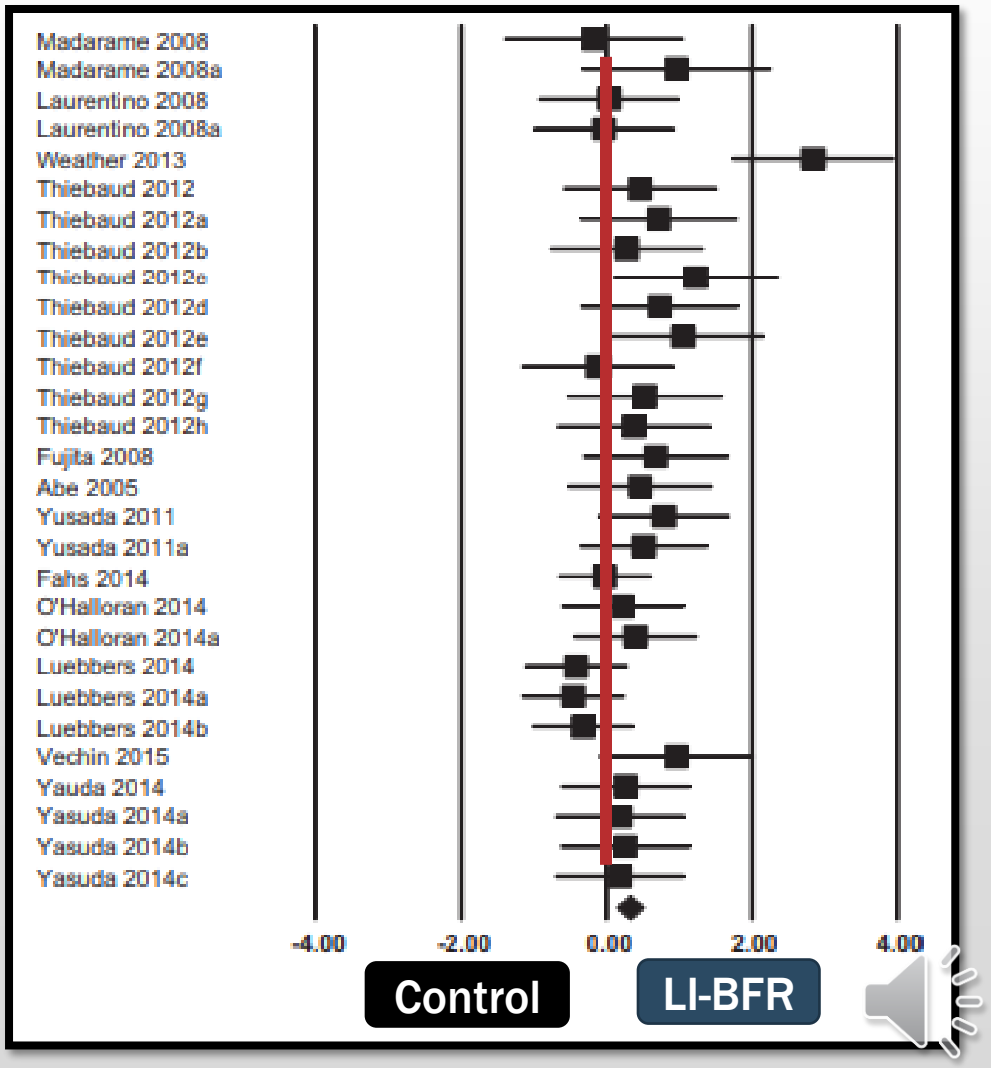
Muscle Strength



Slyzs et al. 2016 [85]

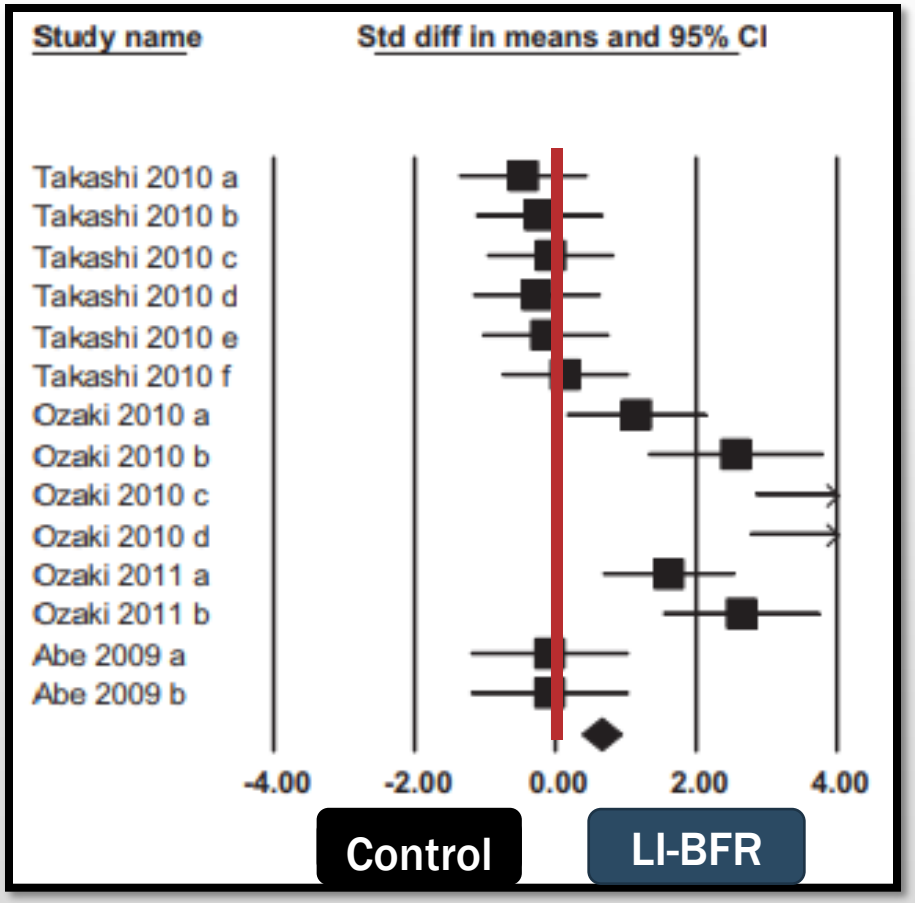
28 Study Meta Analysis

Muscle Hypertrophy

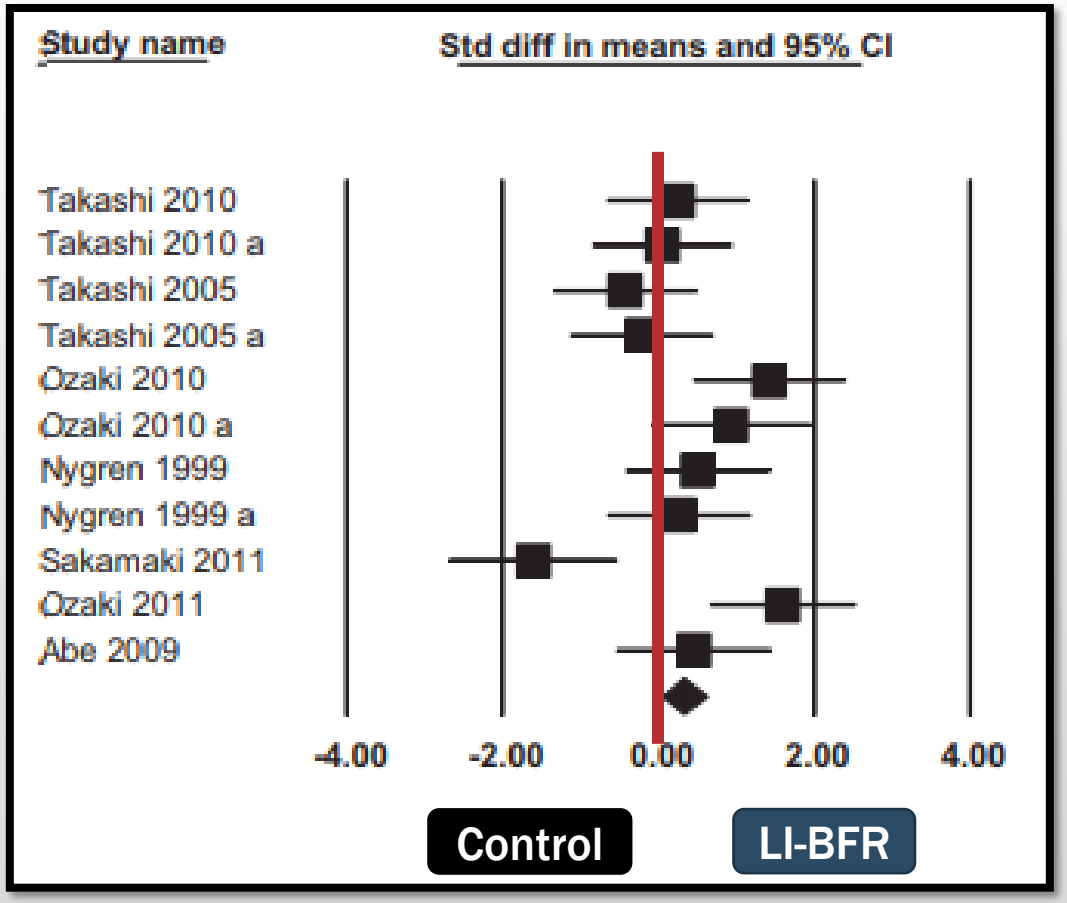


Effectiveness of Blood Flow Restriction - Aerobic

Muscle Strength



Muscle Hypertrophy



Slyzs et al. 2016

Following Topics of Interest:

1. Strength & Blood Flow
2. BFR & Post Surgical Populations
3. BFR & Neurologic Diseases
4. BFR & Muscular Diseases

BFR Effectiveness – Strength & Blood Flow

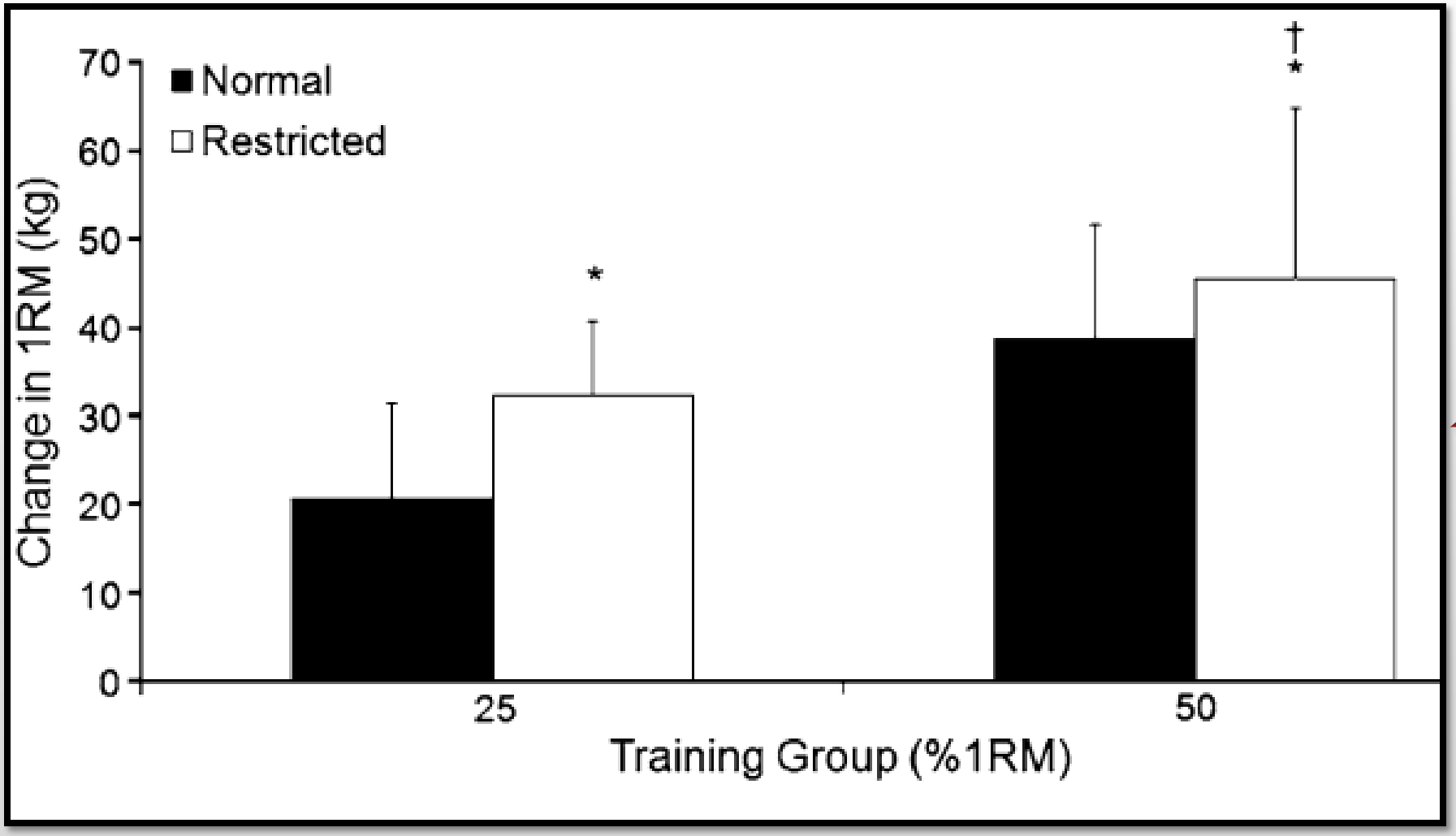
- Subjects: **n = 16 (Female)**
- Exercise: **Unilateral Plantar Flexion**
- Intensity Cohorts: **25% or 50% 1 RM (1 LE BFR, 1 LE no BFR)**
- Duration: **4 weeks, 3x/week, 5-8 min/set**
- Volume: **3 sets to failure (cadence 1.5 sec ↑ & 1.5 sec ↓)**

Outcomes:

- Isokinetic Dynamometer
- **Strength: 1 RM**
- **Isometric MVC**
- **Torque @: 0.52, 1.05, 2.09 rad/sec**
- Blood flow: **pre and post (ml/min/100 ml)**

Patterson et al. 2009

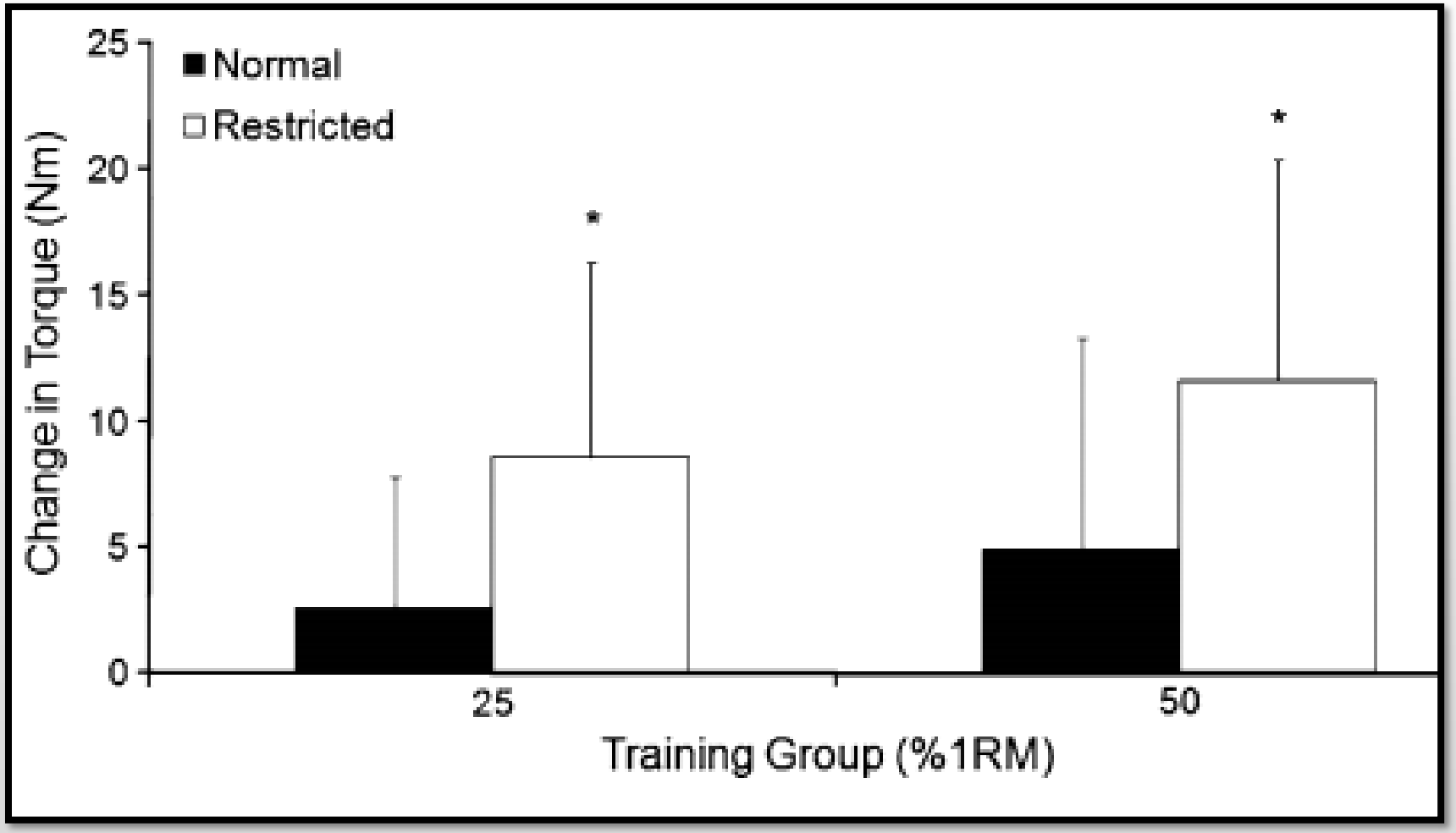
BFR Effectiveness – Strength & Blood Flow



Patterson et al. 2009[98]

26%
1RM

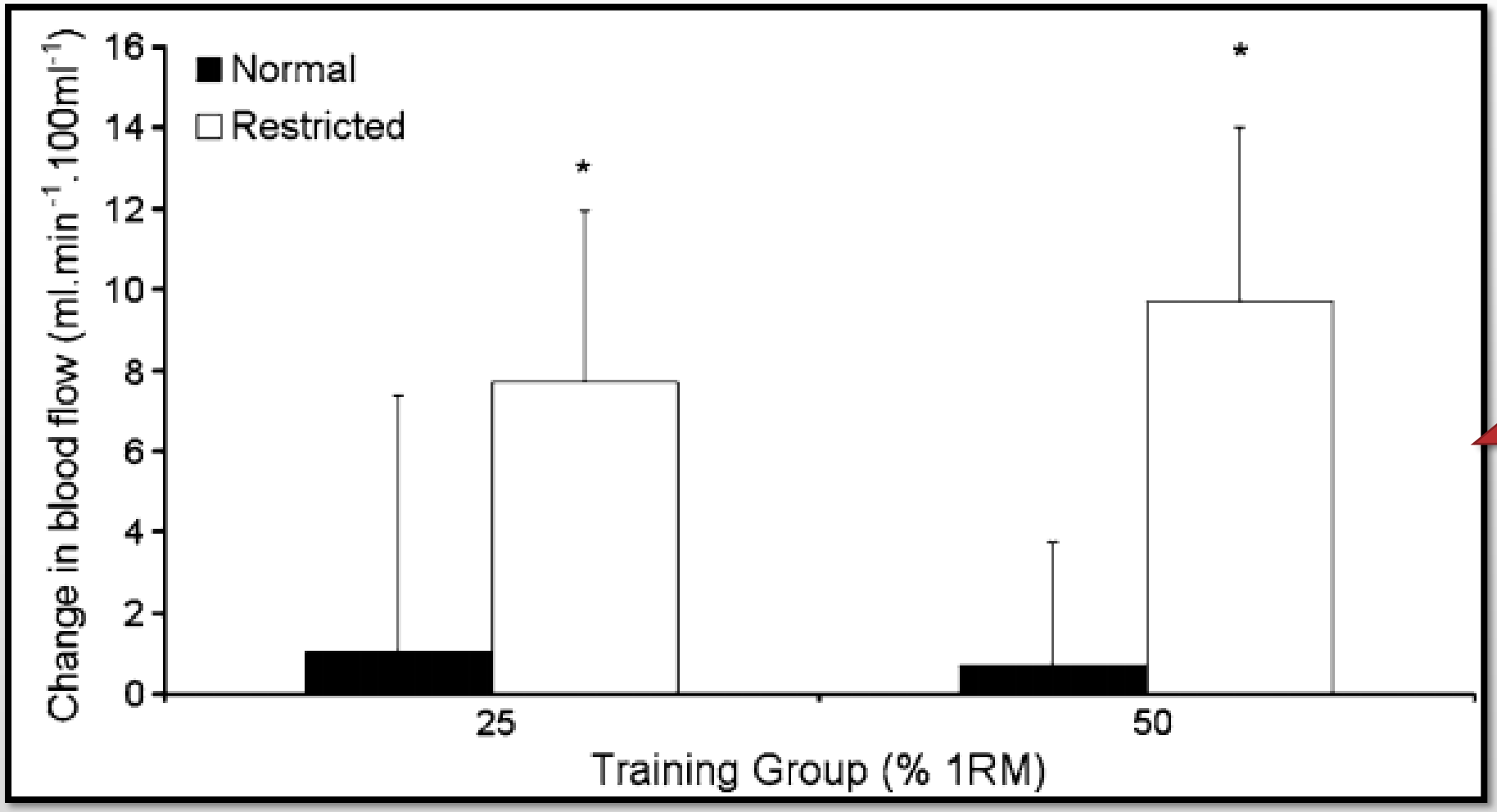
BFR Effectiveness – Strength & Blood Flow



Patterson et al. 2009[98]

106% Iso. MVC

BFR Effectiveness – Strength & Blood Flow



Patterson et al. 2009[98]

43% Blood Flow

Effectiveness of BFR – Post-Operative: Knee Arthroscopy

Method Variable	Value
Subjects	N = 20 (10 BFR; 10 Controls)
Duration	12 Sessions (2 wk post op) 6 weeks
Frequency	~ 2x/week
Type	Control: Post-Op Protocol BFR: Post-Op Protocol + 1. Leg Press 2. Leg Extension 3. Kick Backs
Volume/Intensity	BFR: - 4 sets x 30/15/15/15 - 30% 1 RM - Set rest: 30 sec - Exercise rest: 1 min

Tennet et al. 2018[103]

Blood Flow Restriction Training After Knee Arthroscopy: A Randomized Controlled Pilot Study

Thigh Girth (cm) Proximal to Superior Patellar Pole (cm)†

	P
6-cm proximal	
Occlusion	0.0111*
Control	1
16-cm proximal	
Occlusion	0.0001*
Control	0.1453

Effectiveness of BFR – Post-Operative

Peak Torque (N·m)/Body Weight (kg)

	Final Deficit	*P*	% Improvement Involved
Extension corrected			
Occlusion	23.01 (−9.12 to 64.56)	0.0020*	74.594 (42.16-98.88)
Standard	42.44 (14.348 to 119.71)	0.0156*	33.5 (2.99-51.81)
Flexion corrected			
Occlusion	−2.99 (−18.53 to 10.76)	0.0020*	40.20 (26.7-84.6)
Standard	1.79 (−12.2 to 21.89)	0.0469*	16.80 (0.9-119.3)

Tennet et al. 2018[103]

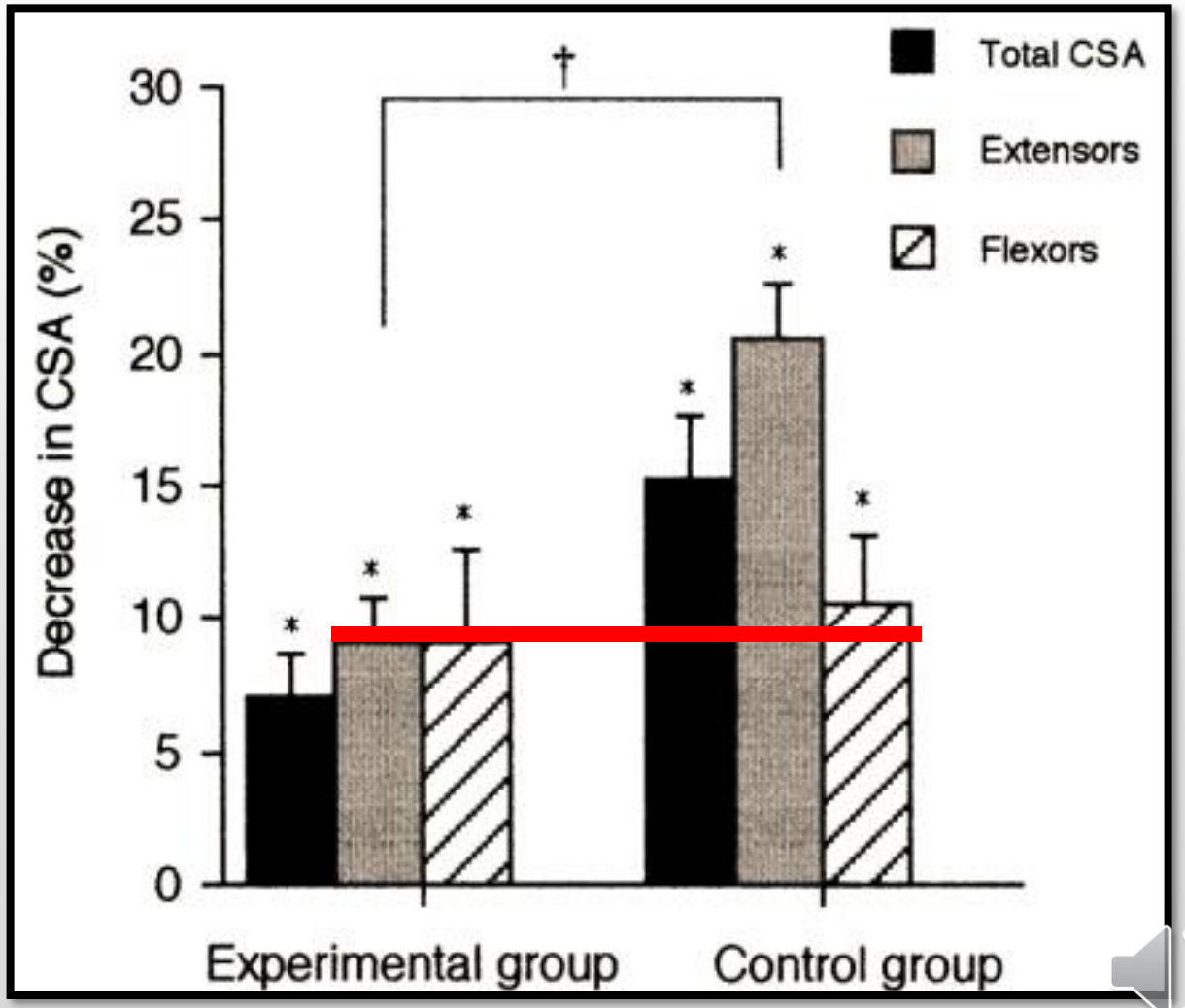
Effectiveness of BFR – Post-Operative: Knee Arthroscopy

Subjective Outcome	BFR	Control
	P	*P*
KOOS		
Pain	0.0001*	0.0412*
Symptoms	0.0028*	0.0781
ADL	0.0009*	0.0844
QOL	0.0034*	0.0755
Sport	0.0009*	0.412*
VR-12		
PCS	0.0098*	0.0451*
MCS	0.0371*	0.4047
Physical outcome		
SSWV	0.0030*	0.0289*
Stair climb	0.0001*	0.2235
FSST	0.0015*	0.0097*
Sit-Stand	0.0107*	0.0062*

Tennet et al. 2018

Effectiveness of BFR – Post-Operative: ACL (1)

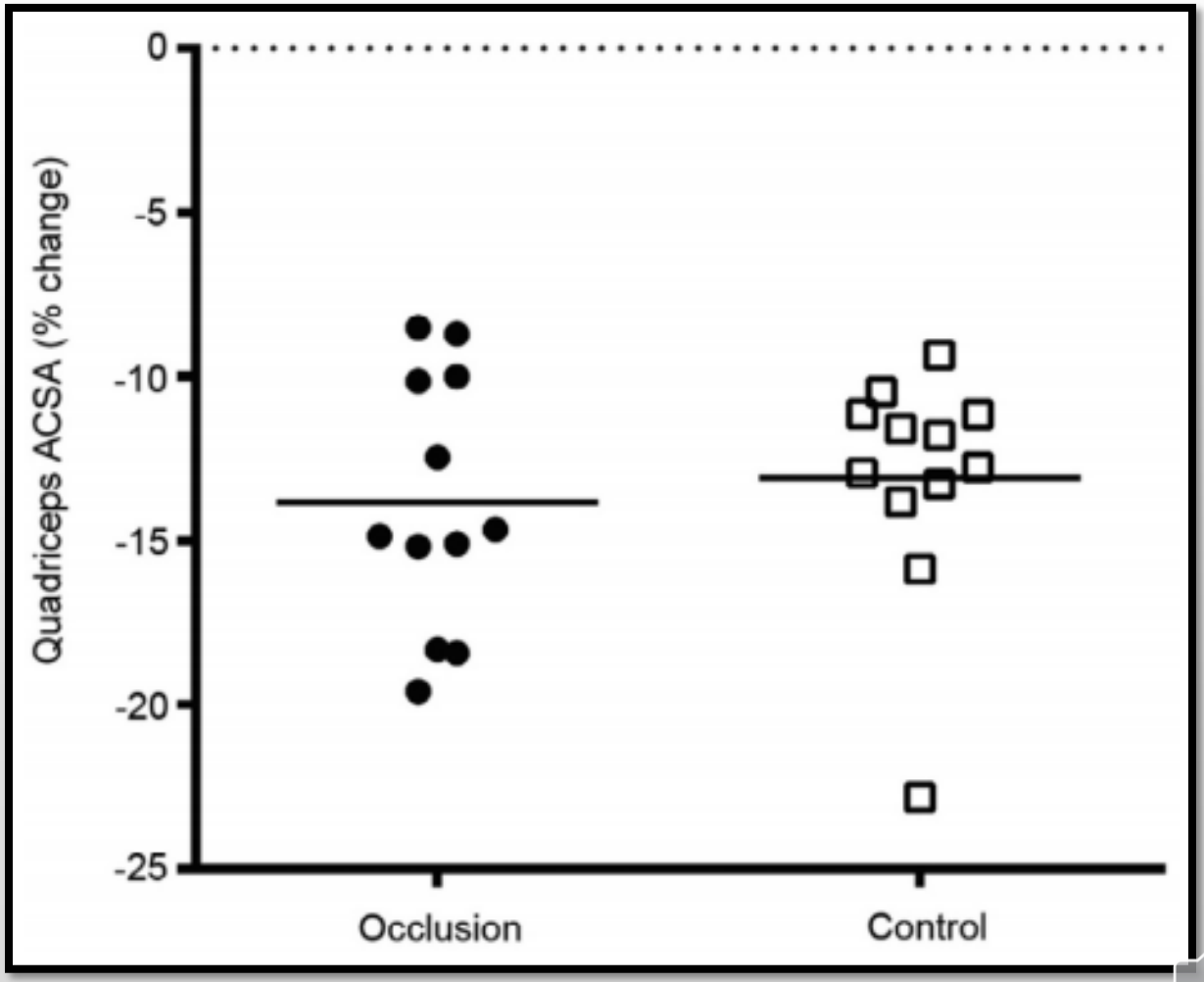
Method Variable	Value
Subjects	N = 16 (8 BFR; 8 Controls) M/F: 8/8 Age: 23 y/o
Duration	2 weeks (Day 3–14 post op)
Cuff	BFR: Width: 90 mm Pressure: 180 mmHg (+10/D) Max Avg: 238 mmHg (210-260) CONTROL: Cuff w/o inflation
Exercise Type	NONE
Frequency	2x/Day
Volume	5x5 min Set Rests: 3 min



Takarada et al. 2000[112]

Effectiveness of BFR – Post-Operative: ACL (2)

Method Variable	Value
Subjects	N = 24 (BFR vs No BFR) M/F: 14/10 Age: 23 y/o
Duration	2 weeks (Day 3–14 post op)
Cuff	BFR: Width: 140 mm Pressure: 130 mmHg (+10/D) Max: 180 mmHg CONTROL: Cuff w/o inflation
Exercise Type	Quad Set (w. towel roll)
Frequency	2x/Day
Volume	5x5 min (5x20 repetitions) Set Rests: 3 min



Iversen et al. 2016[113]

Effectiveness of BFR – Post-Operative: ACL (3)

Method Variable	Value
Subjects	N = 44 (BFR vs No BFR) M/F: 14/10 Age: 29 y/o
Duration	16 weeks
Cuff	BFR: 180 mmHg (operative LE only)
Exercise Type	Post Operative ACL Protocol (see Reference for details)
Frequency	6x/week
Intensity	"Relatively Low"

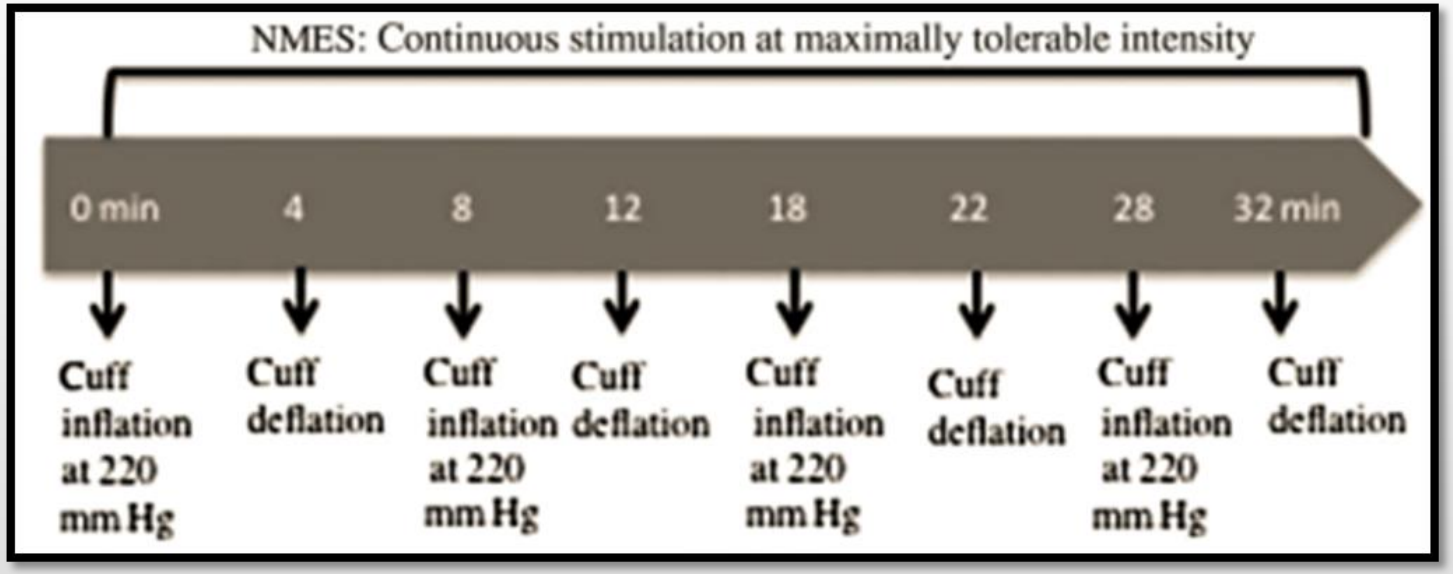
	Before surgery		16 weeks after surgery		p-value
	N group	R group	N group	R group	
Knee extensor muscle strength					
CC60	86 (14)	84 (13)	55 (17)	76 (16)	<0.001
CC180	90 (9)	84 (14)	65 (13)	77 (13)	0.004
IM60	94 (21)	92 (19)	63 (19)	84 (19)	<0.001
Knee flexor muscle strength					
CC60	90 (16)	96 (21)	72 (15)	81 (14)	0.05
CC180	99 (16)	96 (19)	74 (12)	84 (18)	0.04
IM60	94 (17)	91 (18)	62 (14)	72 (11)	0.02

CC60: concentric 60°/sec; CC180: concentric 180°/sec; IM60°

Ohta et al. 2003[114]

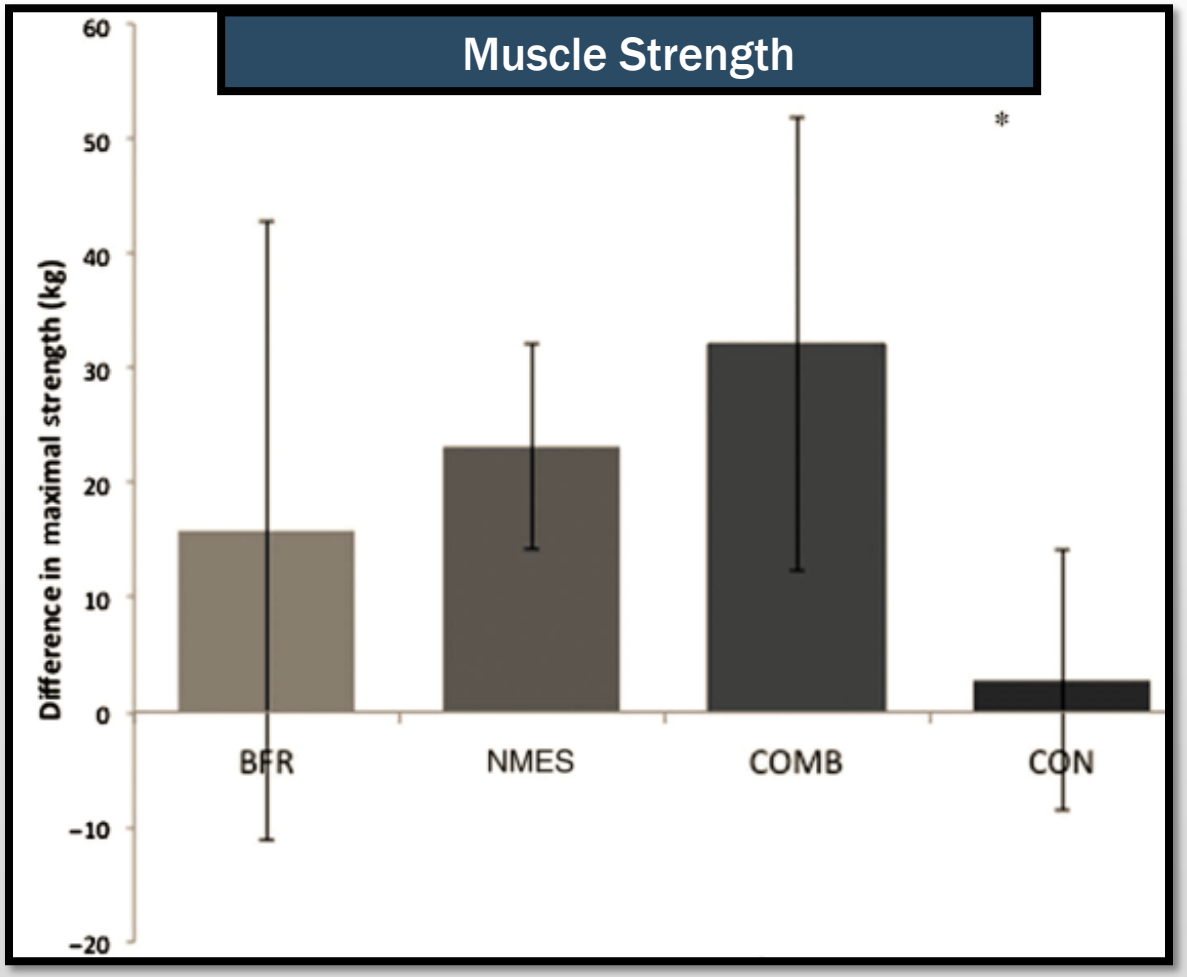
Effectiveness of BFR – Post-Operative: BFR+NMES

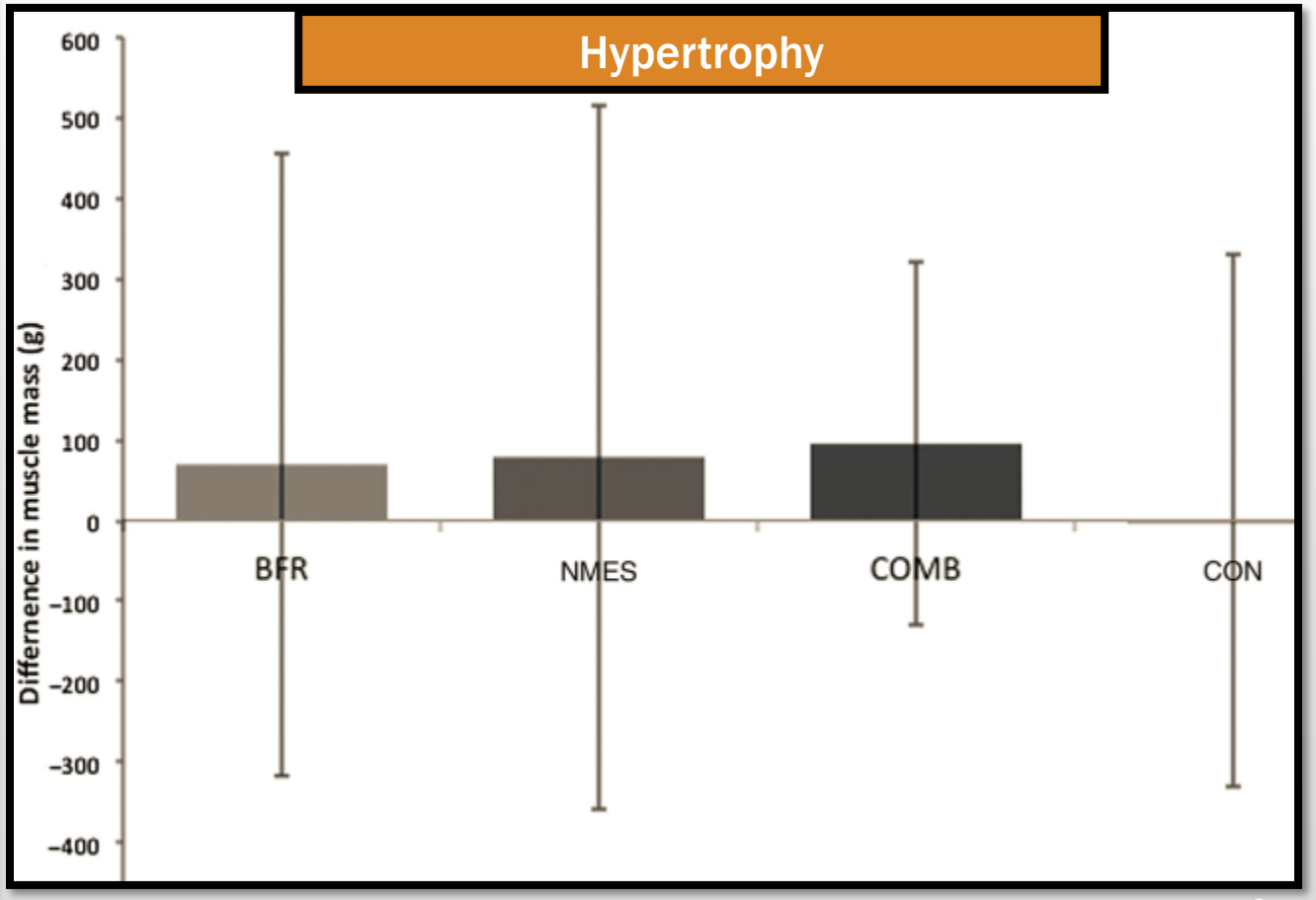
Method Variable	Value
Subjects	N = 20 (M/F: 10/10) Age: 29 y/o
Cohorts	1. Control (CON) | 4. BFR 2. NMES 3. BFR+NMES(COMBO)
Duration	6 weeks
Frequency	4x/week
Cuff	200 mmHg | Width: 10.2 cm 3x4 min inflation
NMES	2 electrodes (5 cm^2) Pulse Length: 400 µs Wave Frequency: 50-100 Hz Intensity: Maximally tolerated



Slysz et al. 2003[115]

Effectiveness of BFR – Post-Operative: BFR+NMES





Slysz et al. 2003

Effectiveness of BFR – Parkinson's Disease

Method Variable	Value
Subjects	N = 1
Duration	10 weeks Phase A: 6 weeks BFR Phase B: 4 weeks no BFR
Time	5x2 min (1 min rest)
Frequency	3x/week
Type	Treadmill Walking
Volume/Intensity	Pace 50m/min 120-160 mmHg

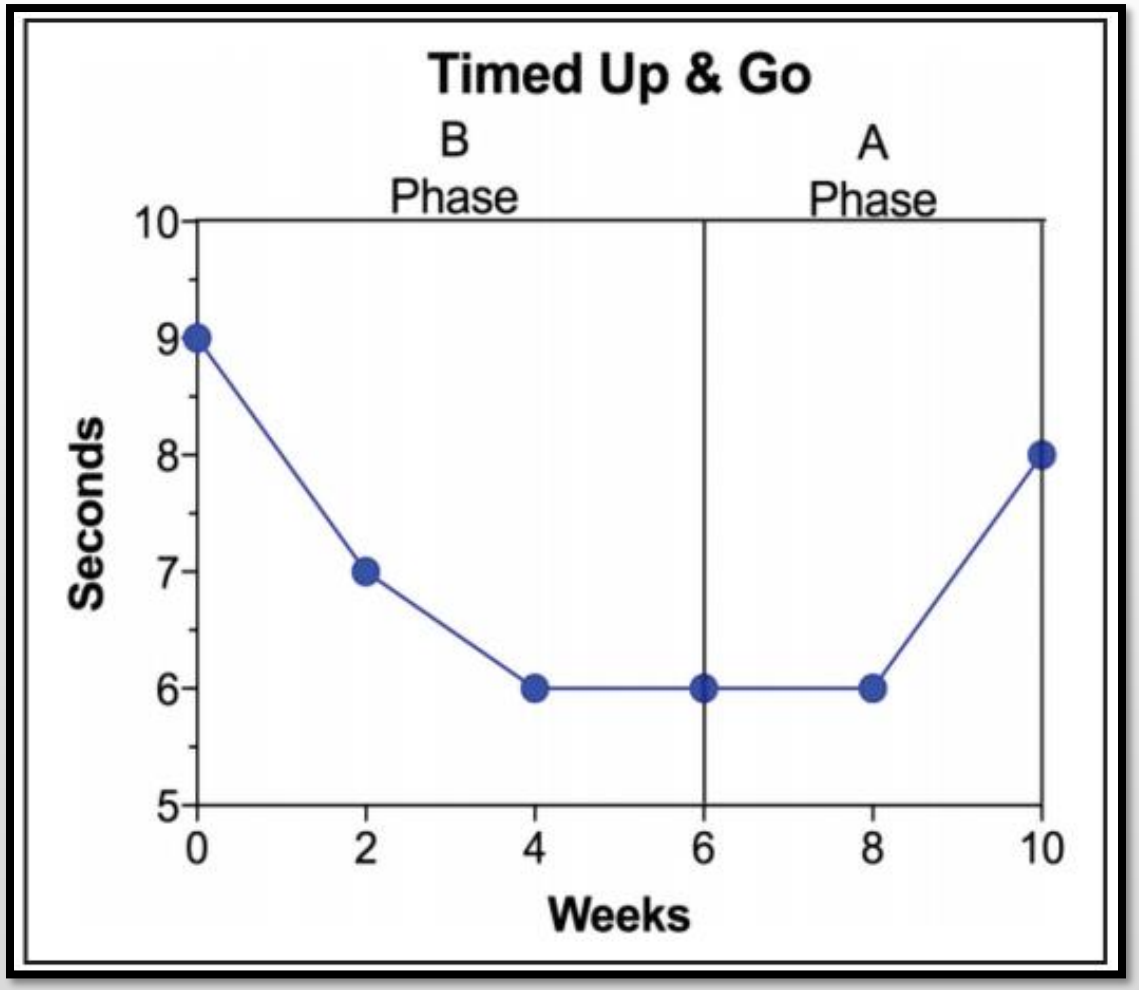
Table 2. *Weekly values for average HR, peak BP and peak RPE.*

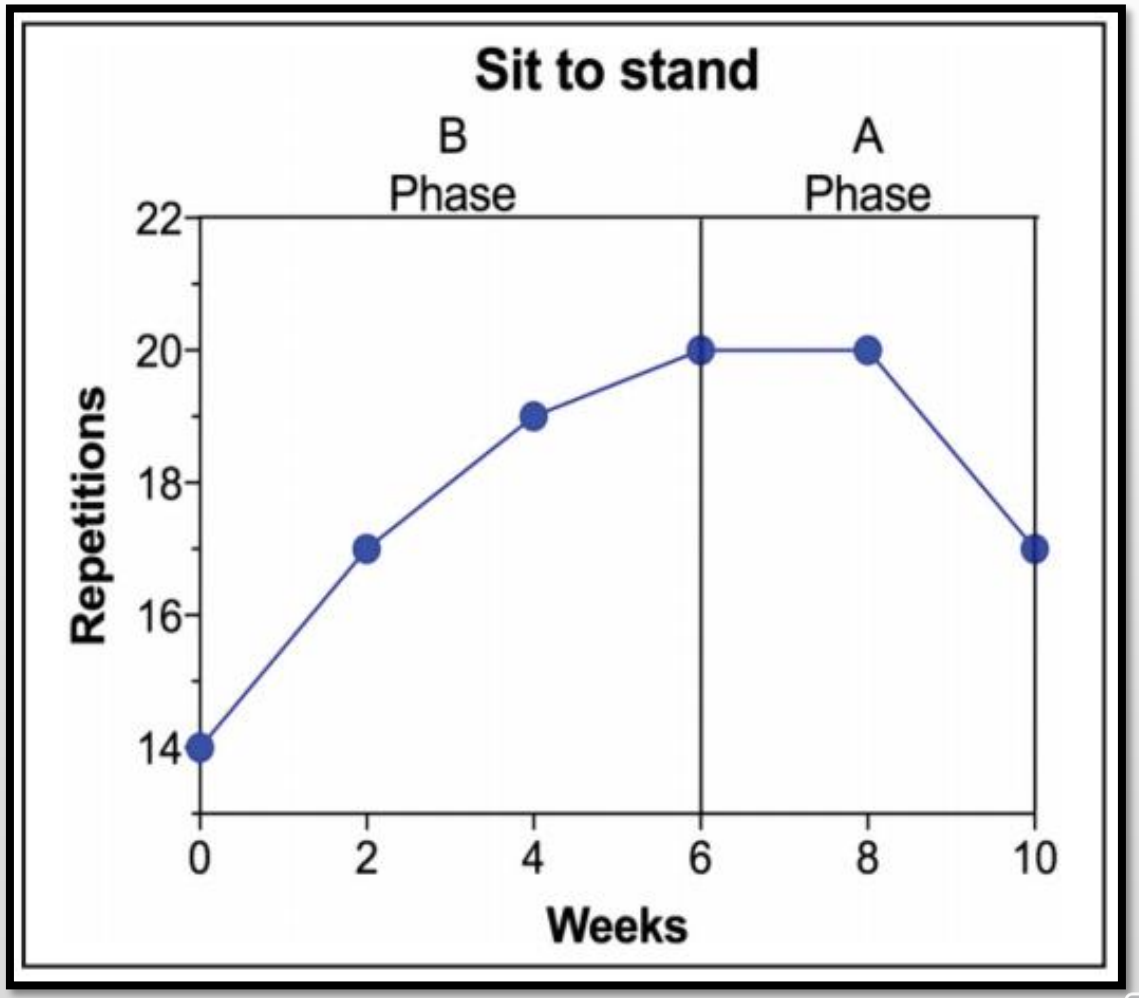
	HR (Mean ± SD)	Peak Weekly BP	Peak RPE
Week 1	68.47 ± 1.71	158/90mmHg	9
Week 2	67.23 ± 1.71	148/78mmHg	7
Week 3	72.99 ± 1.71	142/72mmHg	11
Week 4	69.65 ± 1.71	146/78mmHg	11
Week 5	76.64 ± 1.71	128/74mmHg	10
Week 6	73.27 ± 1.71	150/74mmHg	9

HR, Heart Rate; BP, Blood Pressure; RPE, Rating of Perceived Exertion.

Doris et al. 2018[102]

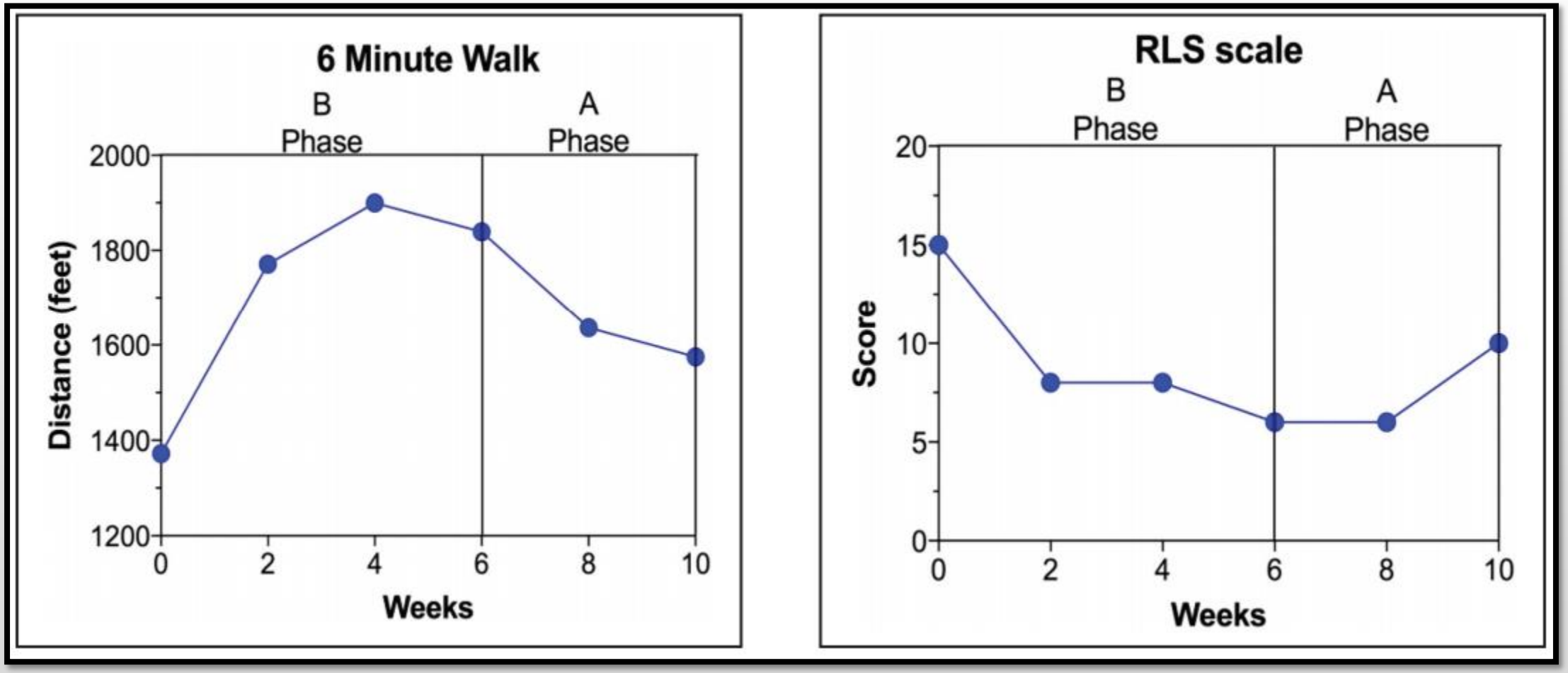
Effectiveness of BFR – Parkinson's Disease





Doris et al. 2018[102]

Effectiveness of BFR – Parkinson's Disease



RLS – resting leg syndrome questionnaire

Doris et al. 2018[102]

Effectiveness of BFR – Polymyositis & Dermatomyositis

Method Variable	Value
Subjects	N = 13
Duration	12 weeks
Time	25-30 min
Frequency	2x/week
Type	Leg Press & Knee Extension
Volume/Intensity	Frequency: 2x/week Week 1: 4x15 @ 20% 1RM Week 2-4: 4x15 @ 30% 1RM Week 5-12: 5x15 @ 30% 1RM

Variable	*P*-value (pre- to post-test)
SF-36 physical function	0.003*
SF-36 role physical	0.041*
SF-36 bodily pain	0.002*
SF-36 general health	0.003*
SF-36 vitality	0.003*
SF-36 social function	0.017*
SF-36 role emotional	0.014*
SF-36 mental health	0.007*
HAQ	0.004*
VAS patient	0.008*
VAS physician	0.004*

Mattar et al. 2014[101]

Effectiveness of BFR – Polymyositis & Dermatomyositis

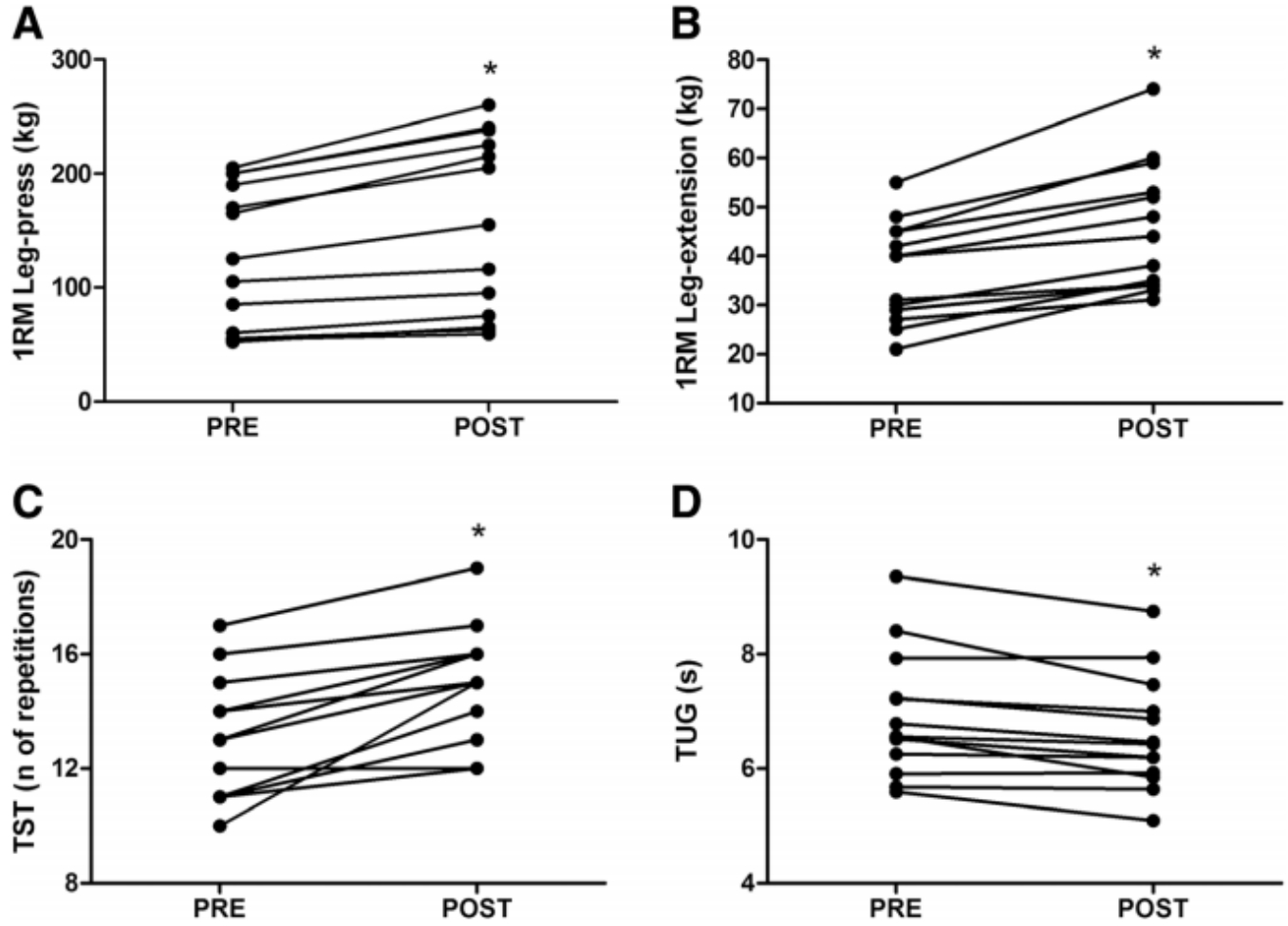


Figure 2 Muscle strength and physical function data at baseline (PRE) and after 12 weeks of intervention (POST). (A) Leg-press exercise one-repetition-maximum (1RM) data; **(B)** knee-extension exercise 1RM data; **(C)** timed-stands test (TST) data; **(D)**: timed up-and-go test (TUG) data. *P <0.05 when compared with baseline assessments.

Mattar et al. 2014

Effectiveness of Blood Flow Restriction - Conclusion

1. LI-BFR: may ↑ in muscle size & strength effects; used when traditional high-load training may be inappropriate or unattainable.
2. 30% 1RM Adaptations > 20% 1 RM Muscle Adaptations
3. Quantifiable muscular adaptations present quickly; Training >6 weeks seem to offer greater returns in strength adaptation.
4. BFR training has applicability to a range of populations who may seek to progress strength while reducing loads on the associated tissues including muscular, tendinous, connective, and bony.

Slyzs et al.[85]

Effectiveness of BFR – Bone Remodeling

Author/Year	Study sample	Intervention type and duration	Conclusion
Beekley *et al.* (2005)	n = 18 healthy men (21–28 years old).	15-min walk (50 m min^{-1}) on the treadmill, 2 × /day, (4-h interval between sessions) for 3 weeks, 6 days $week^{-1}$	Aerobic training combined with BFR, increased the levels of BAP
Bemben *et al.* (2007)	n = 9 active men (18–30 years old).	Two sessions of ST with BFR and control (ST without BFR): 20% 1RM for both groups with a 48-h interval in random order	LI training combined with BFR decreased bone metabolism (NTx) during an acute bout
Karabulut *et al.* (2011)	n = 37 healthy elderly men (58·8 ± 0·6 years old)	ST: 3 × /week for 6 weeks	LISTG showed significant changes in bone ALP concentrations and bone ALP.
Kim *et al.* (2012)	n = 30 healthy untrained men (18–35 years old)	ST: 3 × /week for 3 weeks	HISTG was most effective than LISTG for eliciting bone formation and muscle hypertrophy responses.

Bittar et al. 2018[116]

Effectiveness of BFR – Additional & Future Research

Blood Flow Restriction research is **rapidly expanding.**

Patient demographics in which BFR research has been/will be applied:

1. Post-Operative (Clinical Trials)
   - Lower Extremity: *Knee arthroscopy, ACL, Femur Factures, Achilles tendinopathy, Meniscus repair*
   - Upper Extremity: *distal radius fractures, rotator cuff repair*
   - General: *joint arthroplasty, nerve injuries, muscle strains*
2. Myositis[108]
3. Astronauts[110]
4. Geriatric[104, 106, 107, 109]
5. Adolescent[105]

References

1. Loenneke, Jeremy P., et al. "Blood flow restriction: how does it work?." *Frontiers in physiology* 3 (2012): 392.

2. Takarada, Y., Takazawa, H., and Ishii, N. (2000a). Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Med. Sci. Sports Exerc.* 32, 2035–2039.

3. Takarada, Y., Takazawa, H., Sato, Y., Takebayashi, S., Tanaka, Y., and Ishii, N. (2000b). Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J. Appl. Physiol.* 88, 2097–2106.

4. Yasuda, T., Brechue, W. F., Fujita, T., Shirakawa, J., Sato, Y., and Abe, T. (2009). Muscle activation during low- intensity muscle contractions with restricted blood flow. *J. Sports Sci.* 27, 479–489.

5. Ozaki, H., Sakamaki, M., Yasuda, T., Fujita, S., Ogasawara, R., Sugaya, M., et al. (2011). Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants. *J. Gerontol. A Biol. Sci. Med. Sci.* 66, 257–263.

6. Schliess, F., Richter, L., Vom Dahl, S., and Haussinger, D. (2006). Cell hydration and mTOR-dependent signal- ling. *Acta Physiol. (Oxf.)* 187, 223–229.

7. Suga, T., Okita, K., Morita, N., Yokota, T., Hirabayashi, K., Horiuchi, M., et al. (2010). Dose effect on intramuscular metabolic stress during low-intensity resistance exercise with blood flow restriction. *J. Appl. Physiol.* 108, 1563–1567.

8. Loenneke, J. P., Fahs, C. A., Rossow, L. M., Abe, T., and Bemben, M. G. (2012a). The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. *Med. Hypotheses* 78, 151–154.

9. Loenneke, J. P., Wilson, J. M., Marin, P. J., Zourdos, M. C., and Bemben, M. G. (2012b). Low intensity blood flow restriction training: a meta-analysis. *Eur. J. Appl. Physiol.* 112, 1849–1859.

10. Fry, C. S., Glynn, E. L., Drummond, M. J., Timmerman, K. L., Fujita, S., Abe, T., et al. (2010). Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *J. Appl. Physiol.* 108, 1199–1209.

References

11. Manini, T. M., Vincent, K. R., Leeuwenburgh, C. L., Lees, H. A., Kavazis, A. N., Borst, S. E., et al. (2011). Myogenic and proteolytic mRNA expression follow- ing blood flow restricted exercise. *Acta Physiol. (Oxf.)* 201, 255–263

12. Kubota, A., Sakuraba, K., Koh, S., Ogura, Y., and Tamura, Y. (2011). Blood flow restriction by low compressive force prevents disuse muscular weakness. *J. Sci. Med. Sport.* 14, 95–99.

13. Kubota, A., Sakuraba, K., Sawaki, K., Sumide, T., and Tamura, Y. (2008). Prevention of disuse muscular weakness by restriction of blood flow. *Med. Sci. Sports Exerc.* 40, 529–534.

14. Laurentino, G. C., Ugrinowitsch, C., Roschel, H., Aoki, M. S., Soares, A. G., Neves, M. Jr. et al. (2012). Strength training with blood flow restriction diminishes myostatin gene expression. *Med. Sci. Sports Exerc.* 44, 406–412.

15. Abe, T., Kearns, C. F., and Sato, Y. (2006). Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *J. Appl. Physiol.* 100, 1460–1466.

16. VanWye, William R., Alyssa M. Weatherholt, and Alan E. Mikesky. "Blood Flow Restriction Training: Implementation into Clinical Practice." International journal of exercise science 10.5 (2017): 649.

17. Martín-Hernández, Juan, et al. "Adaptation of Perceptual Responses to Low-Load Blood Flow Restriction Training." Journal of strength and conditioning research 31.3 (2017): 765-772.

18. Kumagai, K., et al. "Cardiovascular drift during low intensity exercise with leg blood flow restriction." Acta Physiologica Hungarica 99.4 (2012): 392-399.

19. Kaufman, Kenton R., et al. "Physiological prediction of muscle forces—I. Theoretical formulation." Neuroscience 40.3 (1991): 781-792.

20. de Freitas, Marcelo Conrado, et al. "Role of metabolic stress for enhancing muscle adaptations: practical applications." World journal of methodology 7.2 (2017): 46.

References

21. Goldberg AL, Etlinger JD, Goldspink DF, et al. Mechanism of work-induced hypertrophy of skeletal muscle. Med Sci Sports. 1975;7(3):185–98.

22. Spangenburg EE, Le Roith D, Ward CW, et al. A functional insulin-like growth factor receptor is not necessary for loadinduced skeletal muscle hypertrophy. J Physiol. 2008;586(1): 283–91. 38.

23. Vandenburgh H, Kaufman S. In vitro model for stretch-induced hypertrophy of skeletal muscle. Science. 1979;203(4377):265–8.

24. Manini TM, Clark BC. Blood flow restricted exercise and skeletal muscle health. Exerc Sports Sci Rev. 2009;37(2):78–85.

25. Suga T, Okita K, Morita N, et al. Intramuscular metabolism during low-intensity resistance exercise with blood flow restriction. J Appl Physiol. 2009;106(4):1119–24.

26. Cook SB, Murphy BG, Labarbera KE. Neuromuscular function after a bout of low-load blood flow-restricted exercise. Med Sci Sports Exerc. 2013;45(1):67–74.

27. Schoenfeld BJ. Potential mechanisms for a role of metabolic stress in hypertrophic adaptations to resistance training. Sports Med. 2013;43(3):179–94.

28. Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. J Strength Cond Res. 2010;24(10):2857–72.

29. Goldspink G. Cellular and molecular aspects of muscle growth, adaptation and ageing. Gerodontology. 1998;15(1):35–43.

30. Zou K, Meador BM, Johnson B, et al. The a7b1-integrin increases muscle hypertrophy following multiple bouts of eccentric exercise. J Appl Physiol. 2011;111(4):1134–41.

31. Adams GR. Invited review: autocrine/paracrine IGF-I and skeletal muscle adaptation. J Appl Physiol. 2002;93(3):1159–67.

32. Tatsumi R, Liu X, Pulido A, et al. Satellite cell activation in stretched skeletal muscle and the role of nitric oxide and hepatocyte growth factor. Am J Physiol Cell Physiol. 2006;290(6):C1487–94.

References

33. Uchiyama S, Tsukamoto H, Yoshimura S, et al. Relationship between oxidative stress in muscle tissue and weight-liftinginduced muscle damage. Pflugers Arch. 2006;452(1):109–16.

34. Takarada Y, Nakamura Y, Aruga S, et al. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol. 2000;88(1):61–5.

35. Takarada Y, Takazawa H, Sato Y, et al. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J Appl Physiol. 2000;88(6): 2097–106. 7.

36. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. Eur J Appl Physiol. 2002;86(4):308–14

37. Loenneke JP, Fahs CA, Rossow LM, et al. The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. Med Hypotheses. 2012;78(1):151–4

38. Febbraio MA, Pedersen BK. Contraction-induced myokine production and release: is skeletal muscle an endocrine organ? Exerc Sport Sci Rev. 2005;33(3):114–9

39. Schiaffino S, Dyar KA, Ciciliot S, et al. Mechanisms regulating skeletal muscle growth and atrophy. FEBS J. 2013;280(17): 4292–314.

40. Kawada S, Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. Med Sci Sports Exerc. 2005;37(7):1144–50.

41. Pope ZK, Willardson JM, Schoenfeld BJ. A brief review: exercise and blood flow restriction. J Strength Cond Res. 2013;27(10):2914–26.

References

43. Pearson, Stephen John, and Syed Robiul Hussain. "A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy." Sports Medicine 45.2 (2015): 187-200.

44. Queme, Luis F., Jessica L. Ross, and Michael P. Jankowski. "Peripheral mechanisms of ischemic myalgia." Frontiers in cellular neuroscience 11 (2017): 419.

45. Ehrnborg C, Rosen T. Physiological and pharmacological basis for the ergogenic effects of growth hormone in elite sports. Asian J Androl 2008; 10: 373–383

46. Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol 2000; 88:61–65

47. Kawada S, Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. Med Sci Sports Exerc 2005; 37: 1144–1150

48. Takano H, Morita T, Iida H, Asada K, Kato M, Uno K, Hirose K, Matsumoto A, Takenaka K, Hirata Y, Eto F, Nagai R, Sato Y, Nakajima T. Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. Eur J Appl Physiol 2005; 95: 65–73

49. Anderson JE, Wozniak AC. Satellite cell activation on fibers: modeling events in vivo – an invited review. Can J Physiol Pharmacol 2004; 82: 300–310.

50. Uematsu M, Ohara Y, Navas JP, Nishida K, Murphy TJ, Alexander RW, Nerem RM, Harrison DG. Regulation of endothelial cell nitric oxide synthase mRNA expression by shear stress. Am J Physiol 1995; 269:C1371– C1378

References

51. Reid MB. Role of nitric oxide in skeletal muscle: synthesis, distribution and functional importance. Acta Physiol Scand 1998; 162: 401–409

52. Snijders, Tim, et al. "Satellite cells in human skeletal muscle plasticity." Frontiers in physiology 6 (2015): 283.

53. Anderson JE. A role for nitric oxide in muscle repair: Nitric oxide-mediated activation of muscle satellite cells. Mol Biol Cell 2000; 11:1859–1874

54. Kraemer, William J., and David P. Looney. "Underlying mechanisms and physiology of muscular power." Strength & Conditioning Journal 34.6 (2012): 13-19.

55. Moritani T, Sherman WM, Shibata M, Matsumoto T, Shinohara M. Oxygen availability and motor unit activity in humans. Eur J Appl Physiol 1992; 64: 552–556

56. Idstrom JP, Subramanian VH, Chance B, Schersten T, Bylund-Fellenius AC. Energy metabolism in relation to oxygen supply in contracting rat skeletal muscle. Fed Proc 1986; 45: 2937–2941

57. Katz A, Sahlin K. Effect of decreased oxygen availability on NADH and lactate contents in human skeletal muscle during exercise. Acta Physiol Scand 1987; 131: 119–127

58. Moritani T, Muro M, Nagata A. Intramuscular and surface electromyogram changes during muscle fatigue . J Appl Physiol 1986 ; 60:1179–1185

59. Takarada Y,Nakamura Y, Aruga S,Onda T, Miyazaki S, Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol 2000; 88:61–65

60. Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J Appl Physiol 2000; 88:2097–2106

61. Takarada Y, Takazawa H, Ishii N. Application of vascular occlusion diminsh disuse atrophy of knee extensor muscles. Med Sci Sports Exerc 2000; 32: 2035–2039

References

62. Wang X, Proud CG. The mTOR pathway in the control of protein synthesis. Physiology (Bethesda) 2006; 21: 362–369

63. Fujita S, Abe T, Drummond MJ, Cadenas JG, Dreyer HC, Sato Y, Volpi E, Rasmussen BB. Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. J Appl Physiol 2007; 103: 903–910

64. Drummond MJ, Fujita S, Takashi A, Dreyer HC, Volpi E, Rasmussen BB. Human muscle gene expression following resistance exercise and blood flow restriction. Med Sci Sports Exerc 2008; 40: 691–698

65. McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. Nature 1997; 387: 83–90

66. McPherron AC, Lee SJ. Double muscling in cattle due to mutations in the myostatin gene. Proc Natl Acad Sci USA 1997; 94: 12457–12461

67. Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, Braun T, Tobin JF, Lee SJ. Myostatin mutation associated with gross muscle hypertrophy in a child. N Engl J Med 2004; 350:2682–2688

68. Mesires NT, Doumit ME. Satellite cell proliferation and differentiation during postnatal growth of porcine skeletal muscle. Am J Physiol Cell Physiol 2002; 282: C899–9

69. McCroskery S, Thomas M, Maxwell L, Sharma M, Kambadur R. Myostatin negatively regulates satellite cell activation and self-renewal. J Cell Biol 2003; 162: 1135–1147

70. Grounds MD, Yablonka-Reuveni Z. Molecular and cell biology of skeletal muscle regeneration. Mol Cell Biol Hum Dis Ser 1993; 3: 210–256

References

71. Dodd S, Hain B, Judge A. Hsp70 prevents disuse muscle atrophy in senescent rats. Biogerontology 2008

72. Senf SM, Dodd SL, McClung JM, Judge AR. Hsp70 overexpression inhibits NF-kappaB and Foxo3a transcriptional activities and prevents skeletal muscle atrophy. FASEB J 2008; 22: 3836–3845

73. Naito H, Powers SK, Demirel HA, Sugiura T, Dodd SL, Aoki J. Heat stress attenuates skeletal muscle atrophy in hindlimb-unweighted rats. J Appl Physiol 2000 ; 88 : 359 – 363

74. Takarada Y, Takazawa H, Ishii N. Application of vascular occlusion diminsh disuse atrophy of knee extensor muscles. Med Sci Sports Exerc 2000; 32: 2035–2039

75. Takarada Y, Tsuruta T, Ishii N. Cooperative effects of exercise and occlusive stimuli on muscular function in low-intensity resistance exercise with moderate vascular occlusion. Jpn J Physiol. 2004;54(6):585–92.

76. Takada S, Okita K, Suga T, et al. Low-intensity exercise canincrease muscle mass and strength proportionally to enhancedmetabolic stress under ischemic conditions. J Appl Physiol.2012;113(2):199–205.

77. Sumide T, Sakuraba K, Sawaki K, et al. Effect of resistanceexercise training combined with relatively low vascular occlusion. J Sci Med Sport. 2009;12(1):107–12.

78. Loenneke JP, Pujol TJ. The use of occlusion training to produce muscle hypertrophy. Strength Cond J. 2009;31(3):77–84.

79. Moore DR, Burgomaster KA, Schofield LM, et al. Neuromuscular adaptations in human muscle following low intensity resistance training with vascular occlusion. Eur J Appl Physiol. 2004;92(4–5):399–406.

80. Kaijser L, Sundberg CJ, Eiken O, et al. Muscle oxidative capacity and work performance after training under local leg ischemia. J Appl Physiol. 1990;69(2):785–7.

References

81. Shinohara M, Kouzaki M, Yoshihisa T, et al. Efficacy of tourniquet ischemia for strength training with low resistance. Eur JAppl Physiol Occup Physiol. 1998;77(1–2):189–91

82. Loenneke JP, Kearney ML, Thrower AD, et al. The acute response of practical occlusion in the knee extensors. J Strength Cond Res. 2010;24(10):2831–4.

83. Heitkamp, H. C. "Training with blood flow restriction. Mechanisms, gain in strength and safety." The Journal of sports medicine and physical fitness 55.5 (2015): 446-456.

84. Loenneke, J. P., R. S. Thiebaud, and T. Abe. "Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence." Scandinavian journal of medicine & science in sports 24.6 (2014): e415-422.

85. Slysz, Joshua, Jack Stultz, and Jamie F. Burr. "The efficacy of blood flow restricted exercise: A systematic review & meta-analysis." Journal of science and medicine in sport 19.8 (2016): 669-675.

86. Loenneke, Jeremy P., et al. "Low intensity blood flow restriction training: a meta-analysis." European journal of applied physiology 112.5 (2012): 1849-1859.

87. Scott, Brendan R., et al. "Exercise with blood flow restriction: an updated evidence-based approach for enhanced muscular development." Sports medicine 45.3 (2015): 313-325.

88. Nakajima, T., Morita, T., Sato Y. “Key Considerations when conducting KAATSU training.” Int. J KAATSU Training Res. 2011; 7:1-6.

89. Yasuda, T, Meguro M, Sato, Y, Nakajima T. “Use and safety of KAATSU training: results of national survey in 2016.” Int. J KAATSU Training Res. 2017; 13:1-9.

References

90. Loenneke JP, Fahs CA, Rossow LM, et al. Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise. Eur J Appl Physiol. 2012;112(8):2903–12.

91. Cook SB, Clark BC, Ploutz-Snyder LL. Effects of exercise load and blood-flow restriction on skeletal muscle function. Med Sci Sports Exerc. 2007;39(10):1708–13.

92. Loenneke JP, Kim D, Fahs CA, et al. Effects of exercise with and without different degrees of blood flow restriction on torque and muscle activation. Muscle Nerve. Epub 2014 Sep 3. doi:10.1002/mus.24448.

93. Wilson JM, Lowery RP, Joy JM, et al. Practical blood flow restriction training increases acute determinants of hypertrophy without increasing indices of muscle damage. J Strength Cond Res. 2013;27(11):3068–75.

94. Loenneke JP, Thiebaud RS, Fahs CA, et al. Effect of cuff type on arterial occlusion. Clin Physiol Funct Imaging. 2013;33(4):325–7

95. Loenneke JP, Thiebaud RS, Fahs CA, et al. Blood flow restriction: Effects of cuff type on fatigue and perceptual responses to resistance exercise. Acta Physiol Hung. 2014;101(2):158–66.

96. Kacin A, Strazar K. Frequent low-load ischemic resistanceexercise to failure enhances muscle oxygen delivery and endur-ance capacity. Scand J Med Sci Sports. 2011;21(6):e231–41.

97. Spranger, Marty D., et al. "Blood flow restriction training and the exercise pressor reflex: a call for concern." American Journal of Physiology-Heart and Circulatory Physiology 309.9 (2015): H1440-H1452.

98. Patterson, Stephen D., and Richard A. Ferguson. "Increase in calf post-occlusive blood flow and strength following short-term resistance exercise training with blood flow restriction in young women." European journal of applied physiology 108.5 (2010): 1025-1033.

References

99. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. J Appl Physiol 58:785–790, 1985

100. Loenneke, J. P., et al. "Potential safety issues with blood flow restriction training." Scandinavian journal of medicine & science in sports 21.4 (2011): 510-518.

101. Mattar, Melina Andrade, et al. "Safety and possible effects of low-intensity resistance training associated with partial blood flow restriction in polymyositis and dermatomyositis." Arthritis research & therapy 16.5 (2014): 473.

102. Douris, Peter C., et al. "THE EFFECTS OF BLOOD FLOW RESTRICTION TRAINING ON FUNCTIONAL IMPROVEMENTS IN AN ACTIVE SINGLE SUBJECT WITH PARKINSON DISEASE." International Journal of Sports Physical Therapy 13.2 (2018).

103. Tennent, David J., et al. "Blood flow restriction training after knee arthroscopy: a randomized controlled pilot study." Clinical Journal of Sport Medicine 27.3 (2017): 245-252.

104. Iida, Haruko, et al. "Effects of walking with blood flow restriction on limb venous compliance in elderly subjects." Clinical physiology and functional imaging 31.6 (2011): 472-476.

105. Luebbers, Paul E., Emily V. Witte, and Johnathan Q. Oshel. "The Effects Of Practical Blood Flow Restriction Training On Adolescent Lower Body Strength." Journal of strength and conditioning research (2017).

106. Ozaki, Hayao, et al. "Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants." Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 66.3 (2010): 257-263.

107. Ozaki, Hayao, et al. "Effects of 10 weeks walk training with leg blood flow reduction on carotid arterial compliance and muscle size in the elderly adults." Angiology 62.1 (2011): 81-86.

References

108. Jørgensen, A. N., et al. "Blood-flow restricted resistance training in patients with sporadic inclusion body myositis: a randomized controlled trial." Scandinavian journal of rheumatology (2018): 1-10.

109. Libardi, C. A., et al. "Effect of concurrent training with blood flow restriction in the elderly." International journal of sports medicine (2015).

110. Hackney, Kyle J., et al. "Blood flow-restricted exercise in space." Extreme physiology & medicine 1.1 (2012): 12.

111. Pinto, Roberta R., et al. "Acute resistance exercise with blood flow restriction in elderly hypertensive women: haemodynamic, rating of perceived exertion and blood lactate." Clinical physiology and functional imaging 38.1 (2018): 17-24.

112. Takarada, Yudai, Haruo Takazawa, and Naokata Ishii. "Applications of vascular occlusions diminish disuse atrophy of knee extensor muscles." Medicine and science in sports and exercise 32.12 (2000): 2035-2039.

113. Iversen, Erik, Vibeke Røstad, and Arne Larmo. "Intermittent blood flow restriction does not reduce atrophy following anterior cruciate ligament reconstruction." Journal of Sport and Health Science 5.1 (2016): 115-118.

114. Ohta, Haruyasu, et al. "Low-load resistance muscular training with moderate restriction of blood flow after anterior cruciate ligament reconstruction." Acta Orthopaedica Scandinavica 74.1 (2003): 62-68.

115. Slysz, Joshua T., and Jamie F. Burr. "The effects of blood flow restricted electrostimulation on strength and hypertrophy." Journal of sport rehabilitation 27.3 (2018): 257-262.

116. Bittar, S. T., et al. "Effects of blood flow restriction exercises on bone metabolism: a systematic review." Clinical physiology and functional imaging (2018).