The Application of Blood Flow Restriction: Lessons From the Laboratory

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Abstract

Blood flow restriction by itself or in combination with exercise has been shown to produce beneficial adaptations to skeletal muscle. These adaptations have been observed across a range of populations, and this technique has become an attractive possibility for use in rehabilitation. Although there are concerns that applying blood flow restriction during exercise makes exercise inherently more dangerous, these concerns appear largely unfounded. Nevertheless, we have advocated that practitioners could minimize many of the risks associated with blood flow-restricted exercise by accounting for methodological factors, such as cuff width, cuff type, and the individual to which blood flow restriction is being applied. The purpose of this article is to provide an overview of these methodological factors and provide evidence-based recommendations for how to apply blood flow restriction. We also provide some discussion on how blood flow restriction may serve as an effective treatment in a clinical setting.

Introduction

Blood flow restriction in combination with low load resistance training (20% to 30% one-repetition maximum [1RM]) has been demonstrated to increase muscle size and strength similar to that observed with traditional high load resistance training (1,2). To induce blood flow restriction, a pneumatic cuff is placed and inflated at the most proximal portion of the upper and/or lower limb(s) which causes arterial blood inflow to be reduced and largely occludes venous return (3). This method has produced favorable muscular adaptations when applied in the absence of muscle contraction (4), throughout the rehabilitation period after surgery (5–7), with low-intensity aerobic exercise (~45% $\dot{V}O_{2max}$) (8) as well as with low load resistance exercise (20% to 30% 1RM) (1). This technique also has demonstrated its effectiveness across a variety of populations, such as the injured (4), healthy individuals (9), elderly (10), athletes (11–13), and has the potential to be efficacious for astronauts (14). A variety of repetition schemes have been employed in the blood flow restriction literature ranging from 45 to 75 repetitions (9,11,15); however, the most commonly used protocol is one set of 30 repetitions followed by three sets of 15 repetitions (75 repetitions) (16).

While blood flow restriction in combination with low load (intensity) training has consistently been shown to be effective for inducing skeletal muscle growth and increasing muscular strength, the safety of this stimulus is repeatedly questioned. Common concerns raised with blood flow-restricted exercise include the potential for increasing the risk of developing a blood clot (17), the augmentation of muscle damage (18), and whether the restriction of blood flow may negatively affect the cardiovascular system (19). Although there are concerns that applying blood flow restriction during exercise makes that exercise inherently more dangerous, this has been largely unfounded in controlled experiments (20,21). Nevertheless, safety and steps to minimize risk should be at the forefront of every practitioners mind when applying this stimulus. We have advocated that practitioners could mitigate many of the risks associated with blood flow-restricted exercise by accounting for methodological factors, such as cuff width, cuff type, and the individual to which the pressure is being applied (22–25). Therefore, the purpose of this article is to provide an overview of these methodological factors and provide evidence-based recommendations for how best to apply blood flow restriction. We also provide some discussion on how blood flow restriction may serve as an effective treatment in a clinical setting (including both postoperative and nonoperative applications).

Applying Blood Flow Restriction

Cuff Width

A range of restrictive cuffs have been applied to restrict blood flow during exercise, such as elastic pneumatic cuffs (11),

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nylon pneumatic cuffs (22), standard blood pressure cuffs (26), and even elastic wraps (27,28). However, a number of these cuffs are of different widths that range from 3 to 18 cm wide (1,25,29). When investigating cuff widths commonly used within the blood flow restriction literature, Loenneke et al. (25) found that a 13.5-cm wide cuff requires less pressure to occlude blood flow than a 5-cm wide cuff in the lower body. Similarly, in the upper body, Jessee et al. (22) found that a 12-cm wide cuff requires less pressure to occlude blood flow compared with 5- and 10-cm wide cuffs. This is important as arbitrary pressures (*e.g.*, 200 mm Hg) used in conjunction with a smaller cuff width are often subsequently used in studies implementing a wider cuff. For example, Abe et al. (30) applied a restriction pressure of 200 mm Hg while using a 5-cm wide cuff, whereas Gundermann et al. (31) applied the same restriction pressure using an 11-cm wide cuff. Although both were inflated to the same absolute pressure, the cardiovascular response to each was potentially quite different.

The need to apply the pressure relative to the cuff width used is perhaps best displayed by Rossow et al. (32). In that study, two different cuff widths were inflated to the same restriction pressure (~150 mm Hg), and it was observed that the 13.5-cm wide cuff induced a greater change in heart rate and blood pressure during exercise than that observed with exercise using a 5-cm wide cuff. Though this would appear to suggest that exercising with wider cuffs would augment the cardiovascular response, it is important to remember that a wider cuff (at subocclusive pressures) inflated to the same pressure as a narrow cuff will always be restricting more blood flow. We have previously shown that exercise with higher relative (% of resting arterial occlusion pressure) restriction pressures produce greater reductions in blood flow (3) and greater increases in blood pressure than exercise with lower relative restriction pressures (33,34). Thus, the greater change in the cardiovascular response is likely due to the greater restriction of blood flow in the 13.5-cm condition, rather than the width of the cuff used per se. In fact, a recent study from our laboratory suggests that when the restriction pressure is made relative to the width of the cuff and the participant, there is a similar reduction in blood flow between 5-, 10-, and 12-cm cuffs (35). To summarize, when care is not taken to apply a pressure relative to the cuff width used, participants' cardiovascular response to exercise may be unnecessarily elevated. Though the magnitude of change in blood pressure is relatively small and returns to baseline relatively quickly after cuff deflation after exercise (36,37), there may be some patient populations where minimizing the cardiovascular response is necessary. For these populations, especially, having an appreciation of the relationship between cuff width and hemodynamic response is essential.

Although there is a similar reduction in blood flow when cuffs are inflated to the same relative pressure, previous literature has suggested that muscle growth may be attenuated directly under the cuff (38,39). Therefore, if one was primarily concerned with muscle growth, then resistance exercising with a narrow cuff (5 cm) may be more favorable compared with a wide cuff (18 cm). For example, Kacin and Strazar (39) examined the muscle growth response in the quadriceps after 4 wk of exercise with (13-cm wide cuff inflated to 230 mm Hg) or without blood flow restriction. There was an overall increase in muscle cross-sectional area of the quadriceps; however, there appeared to be an attenuation of muscle growth directly underneath the cuff where it was positioned. Another study by Ellefsen et al. (38) examined the muscular adaptations to blood flow restriction resistance training and high load resistance training in the lower body for 12 wk. The blood flow restriction condition utilized an 18 cm wide cuff with a restriction pressure of 90 mm Hg to 100 mm Hg. The authors found that both training conditions increased cross-sectional area similarly at the distal location of the quadriceps but observed an attenuation of cross-sectional area at the proximal location in the blood flow restriction condition. Collectively, these studies would suggest that the width of the cuff may impact the amount of muscle growth that occurs in a limb. However, both studies used an arbitrary pressure during blood flow restriction which may have put some individuals under periods of arterial occlusion and/or unnecessarily high pressures. This may have been one reason why muscle growth was attenuated. To help address this, Laurentino et al. (40) compared the muscular adaptation with two distinct cuff widths (5 cm and 10 cm) inflated to a relatively high-restriction pressure (80% arterial occlusion pressure) in the upper body. The authors observed that muscle size increased in a similar manner in both conditions despite the 10-cm cuff covering more area of the limb. This may suggest that applying a relative restriction pressure to the cuff being used can prevent the attenuation of growth under the cuff by ensuring that no one is exercising under complete arterial occlusion. There also may simply be differences between the upper and lower body, given that the previous studies noting the attenuation were completed during lower body resistance exercise (38,39). Lastly, the measurement of one site may have limited the authors' ability to detect an attenuation of growth. Based on the current literature, if an individual wants to maximize growth after blood flow-restricted exercise, we recommend inflating the pressure relative to the cuff width used, and there may be some rationale for applying the pressure over a smaller area.

Cuff Material

The width of the cuff, as discussed in the previous section, is an important factor to consider when applying the restriction pressure (25,32). However, it is important to note that the early studies were not only comparing cuffs of differing width but also of differing material (and often inflation devices). Elastic (11) and nylon (22) are two of the most commonly used cuff materials within the blood flow restriction literature and it was unknown whether the differences between cuffs were due to cuff width or differences in cuff material. When examining the impact of cuff material in the lower body, Loenneke et al. (41) measured resting arterial occlusion pressure using cuffs of similar size (5 cm wide) but different material (nylon vs elastic). The authors found that there were no apparent differences in resting arterial occlusion pressure (41) or repetitions to volitional failure (an indirect marker of blood flow) between cuffs (42). Buckner et al. (29) completed a similar study in the upper body, though the cuffs were of slightly different widths (3 cm elastic vs 5 cm nylon). The authors found that the resting arterial occlusion pressure was much greater in the 3-cm elastic than the 5-cm nylon, and this difference appeared to be driven by more than just the 2-cm difference in cuff width. Regardless of the cuff material, when the restriction pressure was made relative to each cuff, participants completed a similar number of repetitions to volitional failure. This suggested that there appeared to be some differences at rest in the upper body between a 3-cm elastic and a 5-cm nylon cuff, yet these differences appear largely eliminated during exercise when applying the pressure relative to the cuff used.

Individual Characteristics

The restriction pressure applied during blood flow restricted exercise should account for the cuff being used (*e.g.,* cuff width/material) as well as the characteristics of the individual (*e.g.*, limb circumference) to which the pressure is being applied (24). Previous studies suggest that individuals with larger limbs require greater pressures, and those with smaller limbs require lower pressures (22,43). In the upper body especially, an individual's resting blood pressure also will dictate the pressure needed; with higher blood pressures being associated with higher arterial occlusion pressures (22,43). Though associations between brachial blood pressure and arterial occlusion are noted (22,43), investigators should not base lower body blood flow restriction pressure off of blood pressure determined in the brachial artery, given the large difference in limb circumference between the legs and the arms (24). One proposed method that accounts for both the cuff being used and the individual is to apply a percentage of the minimum pressure needed to completely occlude blood flow to a limb in a resting state (*i.e.*, resting arterial occlusion pressure). We hypothesize that this method ensures that all individuals are receiving a similar stimulus and also may reduce the risk of a negative cardiovascular event (19,23). Investigators also may need to measure resting arterial occlusion pressure each training visit rather than applying a restriction pressure based off one time point as arterial occlusion may differ within or across days (44). If investigators are unable to determine resting arterial occlusion pressure directly via a hand-held Doppler probe, they may be able to estimate this pressure using formulas published elsewhere (22,43). As with any equation, they are specific to the cuffs upon which they were developed and do not necessarily translate to other cuff widths.

Exercise Intensity and Restriction Pressure

The appropriate pressure to induce favorable muscle adaptations appears to be dictated, in part, by the exercise load/intensity used. For example, when exercising at 30% to 40% of maximum strength (9,45), a moderate restriction pressure (*e.g.,* 40% arterial occlusion pressure) appears sufficient to induce increases in muscle size and strength with no augmentation in the response by applying a higher restriction pressure (80% to 90% arterial occlusion pressure). This increase in muscle size after moderate restriction pressure is not different from that observed after traditional high load resistance training (45,46). Recent data suggest that if the load is less than 30% of maximum, then a higher restriction pressure (80% arterial occlusion pressure) may be required to induce muscle growth similar to traditional high load resistance exercise (45). If so, higher pressures may be necessary in clinical applications where injury or postoperative restrictions limit the amount of resistance applied. This also may suggest that other lower-intensity exercises, such as walking or cycling, may require higher restriction pressures due to the low force of contractions associated with these movements.

While blood flow restriction is primarily investigated using single joint movements (*i.e.*, elbow flexion and knee extension), it also has been successfully applied to multijoint exercises such as the bench press and squat (11,16). For example, Yasuda et al. (16) examined the muscular response of the pectoralis major and triceps brachii after bench press exercise with or without blood flow restriction and found that the pectoralis major increased in muscle size despite that muscle not being directly restricted. Although there is an increase in muscle growth after blood flow-restricted bench press training, this response is not always to the same extent as that observed after traditional high-load resistance training (47). It has been hypothesized that a greater load and/or number of repetitions may be needed for multijoint exercises to observe favorable muscular benefits when combining blood flow restriction (48). Unpublished observations from our laboratory examined whether the manipulation of load was able to augment the acute muscular response of a muscle (*i.e.*, pectoralis) proximal to the cuff when combined with a moderate restriction pressure (*i.e.*, 40% arterial occlusion pressure). We observed that when the exercise was taken to failure, there were no differences in the proximal and distal acute muscular responses when manipulating the external load (30% 1RM or 50% 1RM). Methodological differences such as the restriction pressure applied (70 mm Hg vs 160 mm Hg) and exercise mode (upright vs supine) could explain the different results compared to Yasuda et al. (16). Though our acute finding should be interpreted with caution given that a training study was not carried out, future investigations may need to apply higher restriction pressures (*i.e.*, 80% arterial occlusion pressure) during compound exercises taken to volitional failure or following the standard protocol.

Practical Blood Flow Restriction

The research on blood flow restriction exercise has primarily been completed using devices capable of regulating the restriction pressure. Although knowing the restriction pressure applied may be critical in research and clinical settings, this may not be a feasible option for the general population exercising at their local gym. A way to apply blood flow restriction during exercise without the use of pneumatic cuffs is through the use of elastic wraps. Elastic knee wraps (~76 mm wide) as an inexpensive, accessible, and practical method of blood flow restriction was first introduced in 2009 by Loenneke and Pujol (49). Following this, several acute studies were performed noting that practical blood flow restriction induced similar changes to those observed when using pressurized cuffs (50–54). However, a limitation of these studies is that the restriction pressure or tightness of the wraps were not quantified.

In an attempt to provide some standard for assessing the pressure applied to a limb with practical blood flow restriction, Wilson et al. (55) developed and implemented a 0 to 10 scale based on perceived tightness. The authors found that everyone in their study still had arterial inflow at a rating of 7 out of 10 on this scale, whereas 67.7% were completely occluded at a 10 of 10. Using this information, the authors had participants exercise with the wraps applied to a 7 of 10 and found acute increases in lactate, muscle swelling, and electromyography amplitude compared to a work-matched control group not exercising with practical blood flow restriction. After this acute work, training studies found that practical blood flow restriction was able to increase muscular strength in athletes in conjunction with their regular resistance training (13,56) and induce muscle growth similar to that observed with traditional high load resistance exercise (57). These results suggest that practical blood flow restriction may be a viable substitute to pneumatic cuffs.

Although these studies using practical blood flow restriction observed benefits, there are some limitations. For instance, Yamanaka et al. (13) and Luebbers et al. (56) did not use a 7 of 10 tightness but instead made marks on the elastic wrap and used a 5- to 7-cm overlap instead. Further, although there have been increases in muscle size and strength with practical blood flow restriction (13,56,57), it is unknown what effect this stimulus has on the veins and arteries. In addition, the 7 of 10 scale was developed on 20 college-aged resistance-trained males and additional work is needed to determine if this scale can appropriately determine the pressure applied in other populations. An alternative to the pressure scale would be to palpate either the radial artery (upper body) or the posterior tibial artery (lower body). If there is no pulse detected, then the wraps are too tight and should be loosened to ensure arterial inflow. While practical blood flow restriction produces favorable muscular adaptations, there are still a lot of unknowns. Future research on practical blood flow restriction needs to be conducted to gain a better understanding on the acute and chronic muscular response as well as the cardiovascular response.

Potential Applications in Clinical Medicine

The application of blood flow restriction may be useful for a number of clinical conditions [please see (58) for a recent systematic review]. However, for the purposes of this review, we have chosen to only highlight a few of the potential clinical applications of this technique.

Postoperative Application

Though rest is necessary, the period of disuse patients experience post-operatively is associated with marked muscle atrophy and strength loss. The loss of muscle cross-sectional area is apparent throughout the stages of rehabilitation and can often persist for months after surgery (59). Muscle weakness also is prevalent after surgery with deficits larger than 20% seen in more than 65% of patients 1-yr after anterior cruciate ligament reconstruction (60). Furthermore, surgeries with more stringent postoperative restrictions, such as cartilage repairs, tendon repairs, and multiligament reconstructions may be at even greater risk for strength and muscle deficits. Targeted postoperative care to mitigate these deficits has become a priority, and rehabilitation protocols that focus on both the cellular and functional level are needed. Preliminary studies support the hypothesis that the application of blood flow restriction by itself (4,61), in combination with neuromuscular electrostimulation (62,63), or in combination with low load resistance exercise (64), may combat many of these deficits normally seen after an operation.

Joint Arthroplasty

Joint arthroplasty surgery typically involves patients beyond the fifth decade of life (65). The advanced age of these patients places them at higher risk of sarcopenic changes and the associated difficulty maintaining muscle cross-sectional area and strength. Additionally, these patients may not tolerate the loads needed for positive muscle adaptation, regardless of their stage of rehabilitation. Given this, the application of blood flow restriction with low load exercise may be efficacious for these patients. In older adults (70 yr), body weight exercise in combination with blood flow restriction has been shown to improve both knee extensor strength and performance in the timed up and go test (66). In addition, exercise with low tension bands in combination with blood flow restriction also has been shown to increase muscle size as well as strength in older adults (67,68). Another potential option may be low-level walking, which when combined with blood flow restriction has been shown to increase muscle adaptation as well as functional performance in the elderly (69,70). Though more work is clearly needed, the application of blood flow restriction with low load (intensity) exercise may be a useful alternative to individuals who may be unable to tolerate traditional high load (intensity) exercise.

Nonoperative Applications

Patellofemoral pain

Patellofemoral pain is one of the most common conditions among active individuals (71). Patellofemoral pain affects those individuals primarily between the ages of 15 and 35 years and has been associated with a higher prevalence in females (72). Although the hallmark symptom is anterior knee pain with loading of the patellofemoral joint, quadricep strengthening is considered a cornerstone of rehabilitation and found to reduce anterior knee pain (73). However, clinicians are often unable to prescribe an adaptive load for quadriceps strengthening without aggravating the patient's symptoms. The addition of blood flow restriction to low load quadriceps exercises for patellofemoral pain is an intriguing concept that may prove to be a solution to the loading conundrum associated with the quadriceps.

There are two stages to consider when rehabilitating individuals with patellofemoral pain; reduction of pain immediately after the treatment session to encourage compliance and improved quadriceps strength along with chronic reduction in pain. Recently, it was observed that low load (30% 1RM) resistance exercise in combination with blood flow restriction reduced pain with daily activities compared with high-load training (70% 1RM) in participants completing treatment for patellofemoral pain (64). Additionally, participants who had pain with resisted knee extension achieved greater gains in quadriceps strength in the blood flow restriction group compared with the standard of care group. After 6 months, both groups were equal on all outcome measures.

Muscle injuries

Muscle injuries are common for those participating in sports (74). Recurrence rates of hamstring injuries have been reported to be as high as 30% (75). A common rehabilitation intervention to prevent and rehabilitate from these injuries is the application of eccentric exercises to the injured muscle group. Unfortunately, many individuals cannot tolerate the eccentric load after injury and loading. Further, the associated muscle soreness post eccentric loading can leave athletes with the feeling of muscle cramping or possibly retearing if they incorporate this training into their in-season program. Given that blood flow restriction is associated with minimal muscle damage (20,76), this technique may be useful for practitioners. However, it is acknowledged that eccentric blood flow restriction exercise does result in some degree of soreness (20 mm of 100 mm on a visual analogue scale) relative to concentric blood flow restricted exercise (76). Furthermore, data on the effectiveness of training only the eccentric portion of the exercise in combination with blood flow restriction is currently limited. The one study that is available suggests that concentric-only blood flow restricted exercise was capable of increasing muscle size and strength, yet this was not observed with eccentric-only blood flow restricted exercise (77). It may be that an individual needs a higher relative load when exercising with "eccentric-only" actions. For example, the eccentric-only condition exercised at 30% of their concentric 1RM which would equate to a much lower relative load within the eccentric portion of the movement. If a higher relative load with eccentric only blood flow restricted exercise is effective, then it may provide the clinician with a suitable alternative to the higher loads most often associated with soft tissue eccentric training. Though we suggest a potential favorable utility of blood flow restriction, whether or not the application of acute blood flow restriction negatively influences the healing time of the tissue directly under or distal to the restriction stimulus also may need to be considered.

Conclusion

The literature on blood flow restriction suggests that this method of training is an effective alternative to traditional high load resistance training. Moreover, blood flow restriction seems to be beneficial during a rehabilitative period and may be useful in the clinical setting. When applying the restriction pressure for blood flow restriction, safety is of the utmost importance. Therefore, investigators should be aware of the effects that cuff width, material, and individual characteristics have on the amount of blood flow being restricted. The pressure should be relative to the cuff used (wider cuff, lower pressure) and to the individual to whom the cuff is being applied (larger limb circumference, greater pressure) rather than applying the same absolute pressure to each individual. The practice of applying the same absolute pressure to everyone should be discontinued, particularly as it relates to the use of blood flow restriction in the clinical setting.

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References

1. Laurentino GC, Ugrinowitsch C, Roschel H, *et al*. Strength training with blood flow restriction diminishes myostatin gene expression. *Med. Sci. Sports Exerc*. 2012; 44:406–12.
2. 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. (1985)*. 2000; 88:2097–106.
3. Mouser JG, Laurentino GC, Dankel SJ, *et al*. Blood flow in humans following low-load exercise with and without blood flow restriction. *Appl. Physiol. Nutr. Metab*. 2017; 1165–71.
4. Takarada Y, Takazawa H, Ishii N. Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Med. Sci. Sports Exerc*. 2000; 32:2035–9.
5. Lejkowski PM, Pajaczkowski JA. Utilization of vascular restriction training in post-surgical knee rehabilitation: a case report and introduction to an under-reported training technique. *J. Can. Chiropr. Assoc*. 2011; 55:280–7.
6. Ohta H, Kurosawa H, Ikeda H, *et al*. Low-load resistance muscular training with moderate restriction of blood flow after anterior cruciate ligament reconstruction. *Acta Orthop. Scand*. 2003; 74:62–8.
7. Tennent DJ, Hylden CM, Johnson AE, *et al*. Blood flow restriction training after knee arthroscopy: a randomized controlled pilot study. *Clin. J. Sport Med*. 2017; 27:245–52.
8. Abe T, Fujita S, Nakajima T, *et al*. Effects of low-intensity cycle training with restricted leg blood flow on thigh muscle volume and VO2max in young men. *J. Sports Sci. Med*. 2010; 9:452–8.
9. Counts BR, Dankel SJ, Barnett BE, *et al*. Influence of relative blood flow restriction pressure on muscle activation and muscle adaptation. *Muscle Nerve*. 2016; 53:438–45.
10. Vechin FC, Libardi CA, Conceição MS, *et al*. Comparisons between low-intensity resistance training with blood flow restriction and high-intensity resistance training on quadriceps muscle mass and strength in elderly. *J. Strength Cond. Res*. 2015; 29:1071–6.
11. Abe T, Kawamoto K, Yasuda T, *et al*. Eight days KAATSU-resistance training improved sprint but not jump performance in collegiate male track and field athletes. *Int. J. KAATSU Train Res*. 2005; 1:19–23.
12. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. *Eur. J. Appl. Physiol*. 2002; 86:308–14.
13. Yamanaka T, Farley RS, Caputo JL. Occlusion training increases muscular strength in division IA football players. *J. Strength Cond. Res*. 2012; 26:2523–9.
14. Loenneke JP, Pujol TJ. KAATSU: rationale for application in astronauts. *Hippokratia*. 2010; 14:224.
15. Madarame H, Neya M, Ochi E, *et al*. Cross-transfer effects of resistance training with blood flow restriction. *Med. Sci. Sports Exerc*. 2008; 40:258–63.
16. Yasuda T, Fujita S, Ogasawara R, *et al*. Effects of low-intensity bench press training with restricted arm muscle blood flow on chest muscle hypertrophy: a pilot study. *Clin. Physiol. Funct. Imaging*. 2010; 30:338–43.
17. Noto T, Hashimoto G, Takagi T, *et al*. Paget-Schroetter syndrome resulting from thoracic outlet syndrome and KAATSU training. *Intern. Med*. 2017; 56:2595-601
18. Iversen E, Røstad V. Low-load ischemic exercise-induced rhabdomyolysis. *Clin. J. Sport Med*. 2010; 20:218–9.
19. Spranger MD, Krishnan AC, Levy PD, *et al*. Blood flow restriction training and the exercise pressor reflex: a call for concern. *Am. J. Physiol. Heart Circ. Physiol*. 2015; 309:H1440–52.
20. Loenneke JP, Thiebaud RS, Abe T. Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence. *Scand. J. Med. Sci. Sports*. 2014; 24:e415–22.
21. Loenneke JP, Wilson JM, Wilson GJ, *et al*. Potential safety issues with blood flow restriction training. *Scand. J. Med. Sci. Sports*. 2011; 21:510–8.
22. Jessee MB, Buckner SL, Dankel SJ, *et al*. The influence of cuff width, sex, and race on arterial occlusion: implications for blood flow restriction research. *Sports Med*. 2016; 46:913–21.
23. Jessee MB, Buckner SL, Mouser JG, *et al*. Letter to the editor: applying the blood flow restriction pressure: the elephant in the room. *Am. J. Physiol. Heart Circ. Physiol*. 2016; 310:H132–3.
24. Loenneke JP, Fahs CA, Rossow LM, *et al*. Blood flow restriction pressure recommendations: a tale of two cuffs. *Front Physiol*. 2013; 4:249.
25. 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; 112:2903–12.

26. Renzi CP, Tanaka H, Sugawara J. Effects of leg blood flow restriction during walking on cardiovascular function. *Med. Sci. Sports Exerc.* 2010; 42:726–32.

27. Loenneke JP, Balapur A, Thrower AD, *et al.* Practical occlusion: a mode to increase low load intensity. *J. Strength Cond. Res.* 2011; 25:S46.

28. Scott BR, Peiffer JJ, Goods PSR. The effects of supplementary low-load blood flow restriction training on morphological and performance-based adaptations in team sport athletes. *J. Strength Cond. Res.* 2017; 31:2147–54.

29. Buckner SL, Dankel SJ, Counts BR, *et al.* Influence of cuff material on blood flow restriction stimulus in the upper body. *J. Physiol. Sci.* 2017; 67:207–15.

30. Abe T, Kearns CF, Sato Y. Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, KAATSU-walk training. *J. Appl. Physiol. (1985)*. 2006; 100:1460–6.

31. Gundermann DM, Fry CS, Dickinson JM, *et al.* Reactive hyperemia is not responsible for stimulating muscle protein synthesis following blood flow restriction exercise. *J. Appl. Physiol. (1985)*. 2012; 112:1520–8.

32. Rossow LM, Fahs CA, Loenneke JP, *et al.* Cardiovascular and perceptual responses to blood-flow-restricted resistance exercise with differing restrictive cuffs. *Clin. Physiol. Funct. Imaging.* 2012; 32:331–7.

33. Jessee MB, Dankel SJ, Buckner SL, *et al.* The cardiovascular and perceptual response to very low load blood flow restricted exercise. *Int. J. Sports Med.* 2017; 38:597–603.

34. Mattocks KT, Jessee MB, Counts BR, *et al.* The effects of upper body exercise across different levels of blood flow restriction on arterial occlusion pressure and perceptual responses. *Physiol. Behav.* 2017; 171:181–6.

35. Mouser JG, Dankel SJ, Jessee MB, *et al.* A tale of three cuffs: the hemodynamics of blood flow restriction. *Eur. J. Appl. Physiol.* 2017; 117:1493–9.

36. Fahs CA, Rossow LM, Seo D-I, *et al.* Effect of different types of resistance exercise on arterial compliance and calf blood flow. *Eur. J. Appl. Physiol.* 2011; 111:2969–75.

37. Rossow LM, Fahs CA, Sherk VD, *et al.* The effect of acute blood-flow-restricted resistance exercise on postexercise blood pressure. *Clin. Physiol. Funct. Imaging.* 2011; 31:429–34.

38. Ellefsen S, Hammarström D, Strand TA, *et al.* Blood flow-restricted strength training displays high functional and biological efficacy in women: a within-subject comparison with high-load strength training. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2015; 309:R767–79.

39. Kacin A, Strazar K. Frequent low-load ischemic resistance exercise to failure enhances muscle oxygen delivery and endurance capacity. *Scand. J. Med. Sci. Sports.* 2011; 21:e231–41.

40. Laurentino GC, Loenneke JP, Teixeira EL, *et al.* The effect of cuff width on muscle adaptations after blood flow restriction training. *Med. Sci. Sports Exerc.* 2016; 48:920–5.

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

42. 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; 101:158–66.

43. Loenneke JP, Allen KM, Mouser JG, *et al.* Blood flow restriction in the upper and lower limbs is predicted by limb circumference and systolic blood pressure. *Eur. J. Appl. Physiol.* 2015; 115:397–405.

44. Ingram JW, Dankel SJ, Buckner SL, *et al.* The influence of time on determining blood flow restriction pressure [Internet]. *J. Sci. Med. Sport* 2017; [cited 2017 Feb 28]. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1440244017302475.

45. Lixandrão ME, Ugrinowitsch C, Laurentino G, *et al.* Effects of exercise intensity and occlusion pressure after 12 weeks of resistance training with blood-flow restriction. *Eur. J. Appl. Physiol.* 2015; 115:2471–80.

46. Kim D, Loenneke JP, Ye X, *et al.* Low-load resistance training with low relative pressure produces muscular changes similar to high-load resistance training. *Muscle Nerve.* 2017; 56:E126-E133.

47. Yasuda T, Ogasawara R, Sakamaki M, *et al.* Combined effects of low-intensity blood flow restriction training and high-intensity resistance training on muscle strength and size. *Eur. J. Appl. Physiol.* 2011; 111:2525–33.

48. Dankel SJ, Jessee MB, Abe T, *et al.* The effects of blood flow restriction on upper-body musculature located distal and proximal to applied pressure. *Sports Med.* 2016; 46:23–33.

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

50. Loenneke JP, Balapur A, Thrower AD, *et al.* Blood flow restriction reduces time to muscular failure. *Eur. J. Sport Sci.* 2012; 12:238–43.

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

52. Loenneke JP, Thrower AD, Balapur A, *et al.* Blood flow-restricted walking does not result in an accumulation of metabolites. *Clin. Physiol. Funct. Imaging.* 2012; 32:80–2.

53. Loenneke JP, Thrower AD, Balapur A, *et al.* The energy requirement of walking with restricted blood flow. *Acta Kinesiol.* 2011; 4:7–11.

54. Loenneke JP, Wilson JM, Balapur A, *et al.* Time under tension decreased with blood flow-restricted exercise. *Clin. Physiol. Funct. Imaging.* 2012; 32:268–73.

55. 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; 27:3068–75.

56. Luebbers PE, Fry AC, Kriley LM, *et al.* The effects of a 7-week practical blood flow restriction program on well-trained collegiate athletes. *J. Strength Cond. Res.* 2014; 28:2270–80.

57. Lowery RP, Joy JM, Loenneke JP, *et al.* Practical blood flow restriction training increases muscle hypertrophy during a periodized resistance training programme. *Clin. Physiol. Funct. Imaging.* 2014; 34:317–21.

58. Hughes L, Paton B, Rosenblatt B, *et al.* Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. *Br. J. Sports Med.* 2017; 51:1003–11.

59. Williams GN, Buchanan TS, Barrance PJ, *et al.* Quadriceps weakness, atrophy, and activation failure in predicted noncopers after anterior cruciate ligament injury. *Am. J. Sports Med.* 2005; 33:402–7.

60. Sachs RA, Daniel DM, Stone ML, *et al.* Patellofemoral problems after anterior cruciate ligament reconstruction. *Am. J. Sports Med.* 1989; 17:760–5.

61. Kubota A, Sakuraba K, Sawaki K, *et al.* Prevention of disuse muscular weakness by restriction of blood flow. *Med. Sci. Sports Exerc.* 2008; 40:529–34.

62. Natsume T, Ozaki H, Saito AI, *et al.* Effects of electrostimulation with blood flow restriction on muscle size and strength. *Med. Sci. Sports Exerc.* 2015; 47:2621–7.

63. Gorgey AS, Timmons MK, Dolbow DR, *et al.* Electrical stimulation and blood flow restriction increase wrist extensor cross-sectional area and flow meditated dilatation following spinal cord injury. *Eur. J. Appl. Physiol.* 2016; 116:1231–44.

64. Giles L, Webster KE, McClelland J, *et al.* Quadriceps strengthening with and without blood flow restriction in the treatment of patellofemoral pain: a double-blind randomised trial. *Br. J. Sports Med.* 2017; 51(23):1688–94.

65. Fang M, Noiseux N, Linson E, *et al.* The effect of advancing age on total joint replacement outcomes. *Geriatr. Orthop. Surg. Rehabil.* 2015; 6:173–9.

66. Yokokawa Y, Hongo M, Urayama H, *et al.* Effects of low-intensity resistance exercise with vascular occlusion on physical function in healthy elderly people. *Biosci. Trends.* 2008; 2:117–23.

67. Yasuda T, Fukumura K, Uchida Y, *et al.* Effects of low-load, elastic band resistance training combined with blood flow restriction on muscle size and arterial stiffness in older adults. *J. Gerontol. A. Biol. Sci. Med. Sci.* 2015; 70:950–8.

68. Thiebaud RS, Loenneke JP, Fahs CA, *et al.* The effects of elastic band resistance training combined with blood flow restriction on strength, total bone-free lean body mass and muscle thickness in postmenopausal women. *Clin. Physiol. Funct. Imaging.* 2013; 33:344–52.

69. Ozaki H, Sakamaki M, Yasuda T, *et al.* 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.* 2011; 66:257–63.

70. Clarkson MJ, Conway L, Warmington SA. Blood flow restriction walking and physical function in older adults: a randomized control trial [Internet]. *J. Sci. Med. Sport* 2017; [cited 2017 Aug 17]. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1440244017303961.

71. DeHaven KE, Lintner DM. Athletic injuries: comparison by age, sport, and gender. *Am. J. Sports Med.* 1986; 14:218–24.

72. Boling M, Padua D, Marshall S, *et al.* Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand. J. Med. Sci. Sports.* 2010; 20:725–30.

73. Crossley KM, van Middelkoop M, Callaghan MJ, *et al.* 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br. J. Sports Med.* 2016; 50:844–52.

74. Elliott MC, Zarins B, Powell JW, *et al.* Hamstring muscle strains in professional football players: a 10-year review. *Am. J. Sports Med.* 2011; 39:843–50.

75. Orchard J, Best TM. The management of muscle strain injuries: an early return versus the risk of recurrence. *Clin. J. Sport Med.* 2002; 12:3–5.

76. Thiebaud RS, Yasuda T, Loenneke JP, *et al.* Effects of low-intensity concentric and eccentric exercise combined with blood flow restriction on indices of exercise-induced muscle damage. *Interv. Med. Appl. Sci.* 2013; 5:53–9.

77. Yasuda T, Loenneke JP, Thiebaud RS, *et al.* Effects of blood flow restricted low-intensity concentric or eccentric training on muscle size and strength. *PLoS One.* 2012; 7:e52843.