Scand J Med Sci Sports 2014: 24: e415–e422
doi: 10.1111/sms.12210

SCANDINAVIAN JOURNAL OF
MEDICINE & SCIENCE
IN SPORTS

Review

Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence

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Accepted for publication 12 February 2014

Blood flow restriction (BFR) alone or in combination with exercise has been shown to result in muscle hypertrophy and strength gain across a variety of populations. Although there are numerous studies in the literature showing beneficial muscular effects following the application of BFR, questions have been raised over whether BFR may lead to or even increase the incidence of muscle damage. The purpose of this review is to examine the proposed mechanisms behind muscle damage and critically review the available BFR literature. The available evidence does not support the hypothesis that BFR in combination with low-intensity exercise increases the incidence of muscle damage. Instead, the available literature suggests that minimal to no muscle damage is occurring with this type of exercise. This conclusion is drawn from the following observations: (a) no prolonged decrements in muscle function; (b) no prolonged muscle swelling; (c) muscle soreness ratings similar to a submaximal low load control; and (d) no elevation in blood biomarkers of muscle damage.

Blood flow restriction (BFR) alone or in combination with exercise has been shown to result in muscle hypertrophy and strength gain across a variety of populations, including the elderly (Abe et al., 2010; Karabulut et al., 2010; Patterson & Ferguson, 2011), highly trained athletes (Takarada et al., 2002), those recovering from injuries (e.g., ACL, osteochondral fracture) (Takarada et al., 2000b; Loenneke et al., 2013b), as well as a patient diagnosed with an idiopathic inflammatory myopathy (Gualano et al., 2010). These muscular benefits have been observed independent of a high load [~ 20–30% concentric one repetition maximum (1RM)] and oftentimes with only BFR in combination with slow walking (Abe et al., 2006). The currently known mechanisms behind these beneficial effects are likely incomplete but are thought to be dependent upon the mode of exercise (i.e., BFR alone vs BFR + aerobic exercise vs BFR + resistance exercise). It has been hypothesized that the foundational mechanism may be the acute increase in muscle cell swelling following the application of BFR alone (Loenneke et al., 2012d) or in combination with aerobic (Ogawa et al., 2012) or resistance exercise (Yasuda et al., 2012). Further proposed mechanisms behind the effects of low load resistance exercise in combination with BFR include increased fiber-type recruitment from metabolic accumulation (Yasuda et al., 2010), decreased myostatin (Laurentino et al., 2012), decreased atrogenes (Manini et al., 2011), and the proliferation of satellite cells (Nielsen et al., 2012).

Although there are numerous studies in the literature showing beneficial muscular effects following the application of BFR, questions have been raised over whether BFR may lead to or even increase the incidence of muscle damage. A large increase in muscle damage would not be favorable for high-frequency training, which is commonly done with BFR (Nielsen et al., 2012). It is important to note that when investigating indirect markers of muscle damage it is important to look at all of the markers collectively as a whole rather than basing the verdict on just one marker. Therefore, the purpose of this review is to briefly discuss proposed mechanisms behind muscle damage and critically review the controlled studies available on BFR.

Mechanisms of muscle damage

In this section, we will briefly discuss possible mechanisms of muscle damage to gain an understanding of what factors may influence the muscle damage response found after BFR resistance exercise. Normal resistance training without BFR can produce significant muscle damage, but the amount and severity of it depends on multiple factors. The type of contraction influences muscle damage such that the eccentric contractions

cause significantly greater muscle damage than concentric contractions (Newham et al., 1983; Nosaka & Newton, 2002). Other mechanical stimuli that initiate muscle damage include the amount of strain placed on individual muscle fibers (Lieber & Friden, 1993), the initial muscle length (Nosaka & Sakamoto, 2001), the force per active area (Black & McCully, 2008), and peak force produced during exercise (McCully & Faulkner, 1986). These factors can be influenced by changing the number, velocity, initial muscle length or the intensity of the exercise. It is interesting to note that when performing the same exercise protocol, the amount of muscle damage increases with increasing intensity such that 40% maximal voluntary contraction (MVC) eccentric contractions produce significantly less muscle damage than 100% MVC eccentric contractions (Chen et al., 2007). Also, little if any muscle damage appears to be produced from low-intensity eccentric contractions (Lavender & Nosaka, 2008). In addition, as the number of lengthening contractions increases, muscle damage increases (Nosaka et al., 2001; Howatson et al., 2007). Therefore, depending on the intensity and number of contractions performed, both of which differ with many BFR resistance training studies, the severity of muscle damage can vary significantly.

All of these stimuli damage the muscle by causing an overstretching of the sarcomere to such an extent that it becomes disrupted, resulting in z-disk streaming and eventually disruption of the cytoskeletal matrix (Proske & Morgan, 2001). Furthermore, muscle damage may result due to activation of stretch-activated calcium channels or transient receptor potential channels (Allen et al., 2005). As these channels become active, intracellular calcium significantly rises above normal levels and activates calcium proteases called calpains, which cleave important cytoskeletal and other sarcomere proteins such as titin, desmin, nebulin, troponin, tropomyosin, kinsases, and more (Allen et al., 2005; Yeung et al., 2005). After the initial damage, inflammation accumulates and more damage may result as the muscle tries to repair the damage (Pizza et al., 2002; Tidball & Villalta, 2010). Ultimately, the symptoms of muscle damage include decreased force production, decreased range of motion, increased muscle soreness, prolonged swelling, increased inflammation, and high levels of creatine kinase and myoglobin in the blood (Clarkson et al., 1986; Nosaka & Clarkson, 1996). The timeline for each marker is slightly different but the most severe declines in force and soreness are found at 24–72 h post-exercise.

With regards to BFR, it has been proposed that the addition of BFR to exercising muscle may result in ischemia-reperfusion muscle damage. Ischemia-reperfusion injury has been examined often in surgical-type experiments. Ischemia-reperfusion involves completely occluding blood flow to a limb during orthopedic, heart, or other surgeries to decrease bleeding. However, in contrast to skeletal muscle, cardiomyocytes are ischemia-intolerant. In skeletal muscle, the amount of damage produced from ischemia-reperfusion is dependent on the duration and severity of ischemia, with irreversible damage being seen between 4 and 6 h of occlusion (Blaisdell, 2002). However, one study has found indications of muscle damage progressing from edema and thickening of the basement membrane at 15 min to invasion of lysosomes, cell degeneration, and cell death in some cells at 90 min (Appell et al., 1993). During this ischemic period, the decrease in muscle oxygen and depletion of energy stores produces a buildup of lactic acid, decreases pH, and if the ischemic conditions are prolonged, cell necrosis can result (Wang et al., 2011). Reperfusion of blood flow to the area then augments this damage due to an increase in reactive oxygen species in the mitochondria (Wang et al., 2011). However, during BFR resistance exercise, the ischemia-reperfusion response is likely minimal compared with surgical experiments due to the fact that blood flow is not completely occluded and exercise typically lasts between 5 and 15 min, followed by complete reperfusion of blood flow.

A review of the evidence

This section will critically review the available evidence on studies whose primary purpose sought to determine whether BFR training produces muscle damage. A breakdown of each study included can be found in Table 1.

Umbel et al. 2009

This investigation included two separate experiments designed to describe the magnitude of delayed-onset muscle soreness (DOMS) associated with BFR exercise, and to determine the contribution of the concentric vs eccentric actions of BFR exercise on DOMS (Umbel et al., 2009). Prolonged swelling, decrements in force, and pain–pressure threshold (PPT) were also investigated as these are all indirect markers of muscle damage. It should be noted that DOMS was based on the participants' general perceived soreness associated with the activities they had performed prior to coming to the laboratory. This retrospective analysis of DOMS is unique but it should be noted that this method is not common throughout the muscle damage literature.

In the first experiment, nine untrained participants performed three sets of unilateral knee extension BFR exercise at 35% of their MVC to failure with a 6-cm wide thigh cuff inflated to 130% above brachial systolic pressure. The participants were given 90 s of rest between sets and each contraction was performed at a 2-s concentric/2-s eccentric cadence. Participants then repeated the protocol with the contralateral limb matching the repetitions completed by the BFR limb; therefore, the control group was not to failure. The study found that mean resting muscle soreness (0–10 scale) 24 h after exercise increased from 0.1 (0.1) to 2.8 (0.3),

Table 1. Overview of studies on blood flow restriction (BFR) and makers of muscle damage

Author	Age	Training status	Protocol	Pressure	Cuff width	Markers used	Conclusions
Umbel et al. 2009	18–34	Untrained	Failure 35% MVC	130% SBP	6 cm	MVC Swelling DOMS PPT	↔ ↔ ↑ ↔
Wernbom et al. 2012	26	Active	Failure 30% 1RM	90/100 mmHg	13.5 cm	MVC Tetranectin DOMS	Unknown ↑ ↑
Loenneke et al. 2013a	19–31	Active	30-15-15-15 30% 1RM	Limb Circ.	5 cm	MVC	↔
Wilson et al. 2013	21	Trained	30-15-15-15 30% 1RM	7/10 PP	7.6 cm	Power Swelling DOMS	Unknown ↔ ↑
Thiebaud et al. 2013	23	Untrained	30-15-15-15 30% 1RM	120 mmHg	3 cm	MVC Swelling DOMS ROM	↔ ↔ ↑ ↔
Takarada et al. 2000a	20–22	Trained	Failure 20% 1RM	214 mmHg	3.3 cm	CK Lipid peroxide IL-6	↔ ↔ ↑
Clark et al. 2011	18–30	Untrained	Failure 30% 1RM	130% SBP	6 cm	CRP	↔
Goldfarb et al. 2008	18–30	Trained	Failure 30% 1RM	SBP*	Not Reported	Protein Carbonyls Glutathione	↔ ↔
Madarame et al. 2013	57	Stable IHD	30-15-15-15 20% 1RM	200 mmHg	5 cm	CRP	↔

*Refers to the cuff being inflated to 20 mmHg below arm SBP for the upper body and to a pressure 40 mmHg above the arm SBP for the lower body. Arrows dictate direction of change from baseline. Unknown was written when reliability of the measurement is unknown.
1RM, one repetition maximum; Circ., circumference; CK, creatine kinase; CRP, c-reactive protein; DOMS, delayed onset muscle soreness; IL-6, interleukin 6; MVC, maximal voluntary contraction; PP, perceived pressure; ROM, range of motion; SBP, brachial systolic blood pressure.

and was 2.4 (0.6) 48 h after BFR exercise to failure with a return to baseline by 96 h. Submaximal exercise without BFR increased from 0.1 (0.1) to 1.7 (0.5) 24 h after exercise and statistically returned to baseline 48 h after 1.4 (0.6) and 0.3 (0.3) at 96 h. Differences existed between groups at 24 h but no differences were found at other time points. For chronic swelling, there was not a condition by time interaction, but there as a time main effect significant increases observed at 24 and 48 h post-exercise. However, these changes were within their error of the measurement (%CV 2.3%); therefore, these differences cannot be considered real. In addition, BFR to failure did not alter the MVC or PPT at any time point compared with baseline nor did submaximal exercise without BFR.

In the second experiment, 15 different untrained participants performed three sets of unilateral BFR exercise at 35% of their MVC with one limb performing only the concentric action and the contralateral limb performing the ECC action. There was 90-s rest between sets with each contraction performed at a 2-s concentric/2-s eccentric cadence with a 6-cm wide thigh cuff inflated to 130% above brachial systolic pressure. Participants performed three sets to failure with the concentric action limb, followed by performing the same number of repetitions with the eccentric action limb. The study found that mean resting muscle soreness (0–10) 24 h after concentric BFR exercise to failure increased from 0.1 (0.1) at baseline to 3.0 (0.5) at 24 h, returning to baseline by 96 h. Submaximal eccentric BFR exercise increased muscle soreness from 0.1 (0.1) at baseline to 1.6 (0.4) at 24 h, returning to baseline by 96 h. Differences between the two muscle actions were observed at 24 h and 48 h post-exercise, with the concentric BFR exercise to failure group demonstrating more soreness than the submaximal eccentric BFR exercise group. For chronic swelling, there was not a condition by time interaction, but there was a time main effect with significant increases observed at 24 h and 48 h post-exercise. However, these changes were within their error of the measurement (%CV 2.3%); therefore, these differences cannot be considered real. There were significant reductions in force 24 h (–99.1 N) following concentric BFR exercise to failure, but this difference returned to baseline by 48 h. Submaximal eccentric BFR exercise did not alter MVC at any time point compared with baseline. In addition, concentric BFR exercise to failure did not alter the PPT at any time point compared with baseline, nor did submaximal ECC exercise with BFR.

In conclusion, experiment 1 found small but significant increases in retrospectively rated DOMS following BFR exercise to failure. Submaximal exercise without BFR also increased DOMS but to a lesser extent. There were no changes from baseline in the remaining variables (i.e., swelling, force, PPT). Experiment 2 found small but significant increases in muscle soreness following concentric BFR exercise to failure and submaximal eccentric BFR exercise; however, the change was greater in the concentric condition which

went to failure. In addition, there was a decrease in force at 24 h post-exercise following concentric BFR exercise to failure although this was not observed following eccentric BFR exercise. Thus, taken together, the majority of indirect markers in this study do not support the hypothesis that muscle damage occurred during conventional exercise (Experiment 1) or when separated out by muscle action (Experiment 2). This appears evident in both experiments, despite comparisons being made between failure and non-failure conditions.

Wernbom et al. 2012

This study sought to investigate muscle function and muscle fiber morphology following a single bout of low load resistance exercise with and without BFR (Wernbom et al., 2012). Twelve physically active participants (8 males/4 females) performed unilateral knee extensions at 30% of their 1RM with an arbitrary pressure applied to the BFR leg (100 mmHg for men, 90 mmHg for women; 13.5-cm wide cuff) and the other leg completed knee extensions without BFR. The BFR leg completed five sets to muscle failure and the free flow leg completed the exact same number of repetitions and sets. There was 45-s rest between sets with each contraction performed at a 1.5-s concentric/1.5-s eccentric cadence. Participants were tested for MVC immediately before, 1 and 2 min post-exercise (with BFR still applied), and at 4, 24, 48, 72, 96, and 168 h post-exercise. DOMS and tetranectin staining of the muscle biopsy were also used as markers of muscle damage. DOMS was self-rated by the participants before the exercise bout and at 4, 24, 48, 72, and 96 h post-exercise on a 10-cm visual analogue scale (VAS). Biopsies were obtained from the vastus lateralis in the free flow leg before exercise and in both legs 1, 24, and 48 h after exercise.

This study found large percentage drops in MVC from baseline immediately post-exercise in both groups; however, the drops were larger in the limb that went to failure with BFR compared with the limb that exercised submaximally without BFR. At no other time point were there differences in the MVC percent change from baseline. Muscle soreness was increased at 24–72 h post-exercise in both limbs and there was no difference between conditions. Collapsed across conditions, the peak muscle soreness was ~ 6 out of 10. The percentage of muscle fibers showing elevated tetranectin staining increased from 9% before exercise to 31% at 1 h, 38% at 24 h, and 27% at 48 h post-exercise in the BFR limb exercising to failure. The limb without BFR exercising submaximally showed an 18% increase in tetranectin staining at 24 h post-exercise. At 24 h, the percentage of muscle fibers with elevated tetranectin staining was significantly greater in the BFR limb exercising to failure compared with the free flow limb completing submaximal exercise.

In conclusion, the study found large acute drops with BFR, which are likely due to fatigue and not muscle damage. The MVC data were presented as percent change rather than raw values; therefore, the magnitude of the effect is unknown, since percent change removes variability from the data (Rhea, 2004). Regardless, the observation that torque was not different at any other time point between conditions suggests that the BFR limb did not receive more damage than the other limb which completed submaximal exercise without BFR. This observation is further confirmed with similar ratings of DOMS between conditions. The tetranectin staining revealed greater and more prolonged staining with the BFR limb, but elevations were still observed in the free flow limb completing submaximal exercise. This observation, taken into context with the physically active population used, calls into question the use of tetranectin as a maker of muscle damage. Interestingly, some evidence suggests that tetranectin may play a role in the fibrinolytic response and may not necessarily be reflective of muscle damage. To illustrate, Hittel et al. (2003) found an exercise-induced increase in both cytoplasmic fluorescence and the number of muscle fibers that stained in a distinct, punctate pattern at or near the plasma membrane. Additionally, their fibrin and gelatin zymography data and expression profile data showed no evidence of muscle damage or regeneration. Taken together with previous research on BFR exercise which has observed increases in fibrinolytic potential (Madarame et al., 2010; Clark et al., 2011), it seems possible and perhaps likely that the elevations in tetranectin staining were a reflection of fibrinolysis and not necessarily of muscle damage or repair. In summation, without the raw values, it is not possible to determine if the drops in MVC were physiologically meaningful or real. DOMS was observed in both groups and this marker by itself may not be a good indicator of muscle damage. Therefore, what can be concluded from this study is that whatever changes occur over time with BFR exercise to failure also occur similarly in the limb performing submaximal exercise without BFR. In fact, previous research from the same group has found that free flow exercise to failure results in greater DOMS than BFR exercise to failure suggesting that exercise, not BFR per se, is producing the DOMS (Wernbom et al., 2009).

Loenneke et al. 2013a

This study sought to determine if BFR (5-cm wide cuff) by itself or in combination with exercise would result in prolonged decrements in torque when using restriction pressures relative to the participant's limb size (bigger limb, greater pressure) (Loenneke et al., 2013a). The protocol used was designed to be submaximal in nature, to try and determine what happens when using a non-failure protocol. This was important as it is not necessary

to train to muscular failure with BFR to see beneficial adaptations (Loenneke et al., 2012f). Although torque was the only indirect marker of muscle damage investigated, it can be argued that it may serve as the best independent predictor of damage (Warren et al., 1999). However, this study would have been much stronger had it included other indirect markers to get a more complete picture of what was happening at the muscle level.

In the first experiment, nine physically active participants (seven males/two females) performed unilateral knee extension at 30% of their 1RM with moderate blood flow restriction on one leg and the other leg completed knee extensions without BFR. The BFR leg completed four sets with the goal repetitions for each set being 30-15-15-15. The BFR leg always went first to ensure the conditions would be repetition matched. Thus, the free flow leg completed the exact same number of repetitions and sets. There was 30-s rest between sets, with each contraction performed at a 1.5-s concentric/1.5-s eccentric cadence. Participants were tested for MVC immediately before, immediately post-exercise (with BFR still applied), and at 1 and 24 h post-exercise. This study found large drops in MVC from baseline in both groups; however, the drops were larger in the limb that exercised with BFR compared with the limb that exercised without BFR. The torque rapidly returned back toward baseline by 1 h in both groups, but it was still slightly reduced in the BFR limb. The torque in both conditions was back to baseline by 24 h post-exercise.

In the second experiment, seven physically active participants (four males/three females) rested for 4 min with BFR applied to one leg and rested for 4 min without any treatment on the other leg. Four minutes was chosen as this would allow time for the limb to be under significant venous pooling. Participants were tested for MVC immediately before, immediately following the final minute of inflation (with BFR still applied), and at 1 and 24 h post-exercise. This study found no drop in MVC from baseline in either group.

In conclusion, the first experiment found that BFR in combination with exercise does not result in prolonged decrements in torque. The large acute drops immediately post-exercise appear to be evidence of fatigue, not muscle damage. It should be mentioned that in contrast to the original purpose, which was to investigate the effects of a non-failure protocol, most of the participants were unable to complete all of the repetitions for the final three sets; therefore, the final sets of resistance exercise were to muscular failure for most in the BFR in combination with exercise condition. Thus, this study cannot definitively say what occurs with BFR in combination with submaximal exercise, as many of the participants were unable to complete the predetermined set of repetitions. This study used a pressure relative to the limb circumference; therefore, part of the discrepancy in repetitions completed is likely due to the pressure used being relative for each individual's limb size (Loenneke et al., 2012c). Furthermore, although 30-15-15-15 has been termed the 'standard' repetition protocol, this is not to say that it is the most optimal protocol. To illustrate, Laurentino et al. (2012) have observed significant increases in muscle size and strength when completing 3–4 sets of 15 repetitions. Furthermore, findings from the second experiment suggest that the application of BFR in the absence of exercise does not result in torque decrements, suggesting that exercise and not BFR per se, is the main driver of fatigue. In summation, this study concludes that BFR, by itself or in combination with resistance exercise, does not result in prolonged decrements in muscle function. However, given that this study did not measure other indirect markers, the study cannot completely rule out muscle damage.

Wilson et al. 2013

This study sought to investigate the acute effects of low intensity practical BFR on muscle damage (Wilson et al., 2013). Practical BFR was first proposed in 2009 (Loenneke & Pujol, 2009), and since then, acute (Loenneke et al., 2012a,e; Wilson et al., 2013) and chronic (Yamanaka et al., 2012; Loenneke et al., 2013b) data show that applying knee wraps in place of the pressurized cuffs may respond similarly to the more expensive devices. Twelve trained male participants completed a 30-15-15-15 repetition scheme at 30% of their leg press 1RM under free flow and BFR conditions in a randomized cross-over design with each condition separated by at least 72 h. The 7.6-cm wide wraps were applied by the same investigator to a rating of 7 out of 10 on a perceived pressure scale. Furthermore, a rating of 7 out of 10 was verified to cause venous but not arterial occlusion in all participants examined in this study. A timed rest period length of 30 s was used between all sets. Prolonged swelling, decrements in power (i.e., vertical jump), and DOMS (VAS scale, 0–10 cm) were investigated as the indirect markers of muscle damage.

The study found that muscle thickness was significantly elevated above baseline immediately post-exercise (wraps still applied) through 5 min post without wraps in the BFR condition. No changes were observed in the control condition. By 24 h post, no swelling existed in either condition. There were no median differences between BFR and control in DOMS at baseline or 24 h post-exercise. The 25th–50th–75th percentiles for DOMS at 24 h were 1–1–2.8 cm and 0–1–2.7 cm, for BFR and control conditions, respectively. Similarly, there was a time effect for peak power, which decreased from pre to 24 h post-training, but no differences existed between conditions.

In conclusion, this study found acute swelling immediately post-exercise in the BFR condition, which appears to be related to a short-term BFR-induced fluid shift. This short-term fluid shift has been previously hypothesized as a possible foundational mechanism

behind the observed benefits of BFR on muscle (Loenneke et al., 2012b) and bone (Loenneke et al., 2012g). The finding that this swelling was acute and not chronic suggests that this marker was not indicating muscle damage. In addition, DOMS was also not different between conditions. This study is unique in that it investigated DOMS using a non-parametric test, which appears to be the most appropriate given the VAS is not continuous variable but is more categorical in nature. However, although the conditions were randomized, the repeated bout effect cannot be ruled out and may have attenuated ratings on the condition completed second (McHugh, 2003). This studies marker of performance showed decrements at 24 h post, but there was no difference between conditions. One limitation in interpreting the power measurement is that true reliability of the measurement is not known. This study reported the Pearson *r* as reliability; however, the Pearson *r* cannot detect systemic variability and is discouraged as a measure of test-retest reliability (Weir, 2005). Nevertheless, peak power returned to within 5% of baseline at 24 h post, suggesting that the difference between time points may not be meaningful. Regardless, measurements past 24 h would have been interesting to see if recovery was similar or different between conditions. In summation, this study suggests that the indirect markers used in this study do not support the hypothesis that muscle damage occurred during low load BFR exercise or low load conventional exercise without BFR.

Thiebaud et al. 2013

This study sought to investigate the effects of submaximal upper body resistance exercise in combination with BFR separated out by muscle action (BFR concentric vs BFR eccentric) (Thiebaud et al., 2013). Ten untrained males had arms randomly assigned to either concentric BFR or eccentric BFR dumbbell curl exercise at 30% of their concentric 1RM. Participants completed four sets of exercise with the 'standard' rep scheme of 30-15-15-15. There was a 30-s rest between sets, with each contraction performed at a 1.5-s concentric/1.5-s eccentric cadence. The BFR pressure was 120 mmHg applied with a 3-cm wide cuff. The indirect markers of muscle damage measured included elbow flexor MVC, circumference of the upper arm, range of motion of the elbow joint, muscle thickness, and muscle soreness on a 100 mm VAS scale. These measurements were taken before, immediately post-exercise (without cuff), and daily for 4 days after the exercise bout of each arm.

The study found significant drops in MVC immediately post-exercise in both groups; however, the decrease was larger with the concentric BFR condition. MVC returned to baseline by 24 h post-exercise. The circumference of the upper arm was acutely increased post-exercise only in the concentric BFR condition; however, this value returned to baseline by 24 h post-exercise. Range of motion was significantly decreased in both conditions immediately post-exercise but returned to baseline by 24 h post-exercise. There was no significant difference between muscle actions. Muscle thickness was acutely increased at the 50% site only in the concentric BFR condition. At the 10-cm muscle thickness site, there were significant increases in both conditions; however, the increases were greatest with the concentric BFR condition. The swelling from both sites returned back to baseline by 24 h post-exercise. When examining changes in muscle soreness, the concentric BFR condition did not increase over time, with the highest value reaching 4 mm at 24 h post-exercise. In the eccentric BFR condition, muscle soreness significantly increased to 20 mm at 24 h and 15 mm at 48 h but was not back to baseline by 72 h.

In conclusion, other than muscle soreness, there were no significant differences in the other variables from baseline at 24, 48, 72, or 96 h post-exercise, indicating that all of the changes were acute and likely not indicative of muscle damage. Muscle soreness although elevated was very low and peaked at 20 mm on a 100 mm scale in the BFR eccentric condition. As stated earlier, the acute drops in MVC are due to fatigue and the acute swelling response may be mechanistically important for adaptation from the BFR stimulus (Loenneke et al., 2012b,g). From the current study, it is not possible to determine if BFR itself is causing the small increase in soreness or if it is due to the exercise itself. However, we have since tried to investigate this (eccentric vs BFR eccentric) using similar methods, but were unable to replicate the increase in muscle soreness (Thiebaud RS, Unpublished observations). In summation, this study found that completing a submaximal protocol previously found to increase muscle size and strength (Yasuda et al., 2012) is not likely to result in muscle damage based on the indirect markers used in this study.

Other acute studies

Although we chose to only focus and critically analyze the studies whose main purpose was to investigate the acute muscle damage response to BFR exercise, we would be remiss if we excluded several other studies that have secondarily looked at acute blood markers of muscle damage. To illustrate, the appearance of creatine kinase in serum would be suggestive of muscle membrane damage; however, increases in this biomarker have not been observed following BFR exercise (Takarada et al., 2000a). Additionally, an increase in oxidative stress and inflammatory markers may also indicate muscle damage; however, increases have also not been observed in these biomarkers with BFR exercise (Takarada et al., 2000a; Goldfarb et al., 2008; Clark et al., 2011; Madarame et al., 2013). A small elevation in IL-6 has been observed (Takarada et al., 2000a), but this is unlikely to be related to muscle damage (Pedersen, 2011). This is because the main source of plasma IL-6 from exercise is not from

macrophages but from muscle contraction itself (Pedersen & Fischer, 2007). However, one potential limitation of these studies is the lack of time course across days. It may be possible that changes in these variables may be seen if the time course was extended.

Perspective

The available evidence does not support the hypothesis that BFR in combination with low-intensity exercise increases the incidence of muscle damage. Instead, the current literature suggests that minimal to no muscle damage is occurring with this type of exercise. This conclusion is drawn from the following observations: (a) no prolonged decrements in muscle function; (b) no prolonged muscle swelling; (c) muscle soreness ratings similar to a submaximal low load control; and (d) no elevation in blood biomarkers of muscle damage. We wish to suggest that BFR in combination with exercise can be completed without a concern for producing major indices of muscle damage.

Key words: KAATSU, MVC, strength, swelling, ROM.

Acknowledgements

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this manuscript. This study was not supported by any funding.

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