Skeletal muscle hypertrophy is defined as an increase in muscle mass, which is an increase in the size rather than the number of skeletal muscle fibers. Signaling cascades and growth factors such as Insulin-like Growth Factor-1 (IGF-1) have been demonstrated to induce skeletal muscle hypertrophy.1,2,3,4
The fields of exercise physiology and molecular biology both have independently demonstrated that in order to achieve hypertrophy, muscle fibers must undergo mechanical stress. It has been hypothesized that mechanoreceptors on myocytes may trigger the IGF-1 signaling cascade for hypertrophy. Hence, the American College of Sports Medicine guidelines recommend a muscle should be stressed with a load between 60 percent and 100 percent of the one repetition maximum to obtain increased muscle strength.

Postoperative limitations on weight bearing status and the physical inability to perform the required mechanical stress leads to muscular atrophy in knee arthroscopy patients. In chronic unloading states the loss of muscle mass is caused by multiple factors including down regulation of the hypertrophic signaling pathway and activation of intracellular signaling cascades that cause muscle protein degradation.

Blood flow restriction (BFR) as a modification to traditional exercise modalities, such as resistance training or walking has become an area of research interest. In Japan, a form of restricting muscular blood flow during resistance training termed KAATSU training demonstrated muscle hypertrophy and increased strength. The technique utilizes the application of pneumatic cuff, similar to a blood pressure cuff, on the proximal aspect of an upper or lower extremity. A selected pressure is used to provide venous occlusion to the distal aspect of the limb. The patient then performs resistance exercises at approximately 20 percent to 30 percent of one repetition maximum.

BFR creates an anaerobic environment. At the lower oxygen tension level the body recruits muscle fibers normally reserved for more strenuous exercise. In return the mechanical stress on the muscle fibers leads to up-regulation of the muscle hypertrophy-signaling cascade.

BFR has quickly gained interest as an exercise technique and could be a revolutionary tool to decrease the time to return to sport postoperatively.

**Review of Current Methodologies and Applications**

Early application of BFR training was demonstrated in the geriatric population in efforts to address age related cardiovascular changes and muscle atrophy. Abe et al. performed a randomized prospective study (n=19) of males and females, age 60 to 78 years old. These patients were randomized to a KAATSU-walk training group or a non-exercising control group. The exercise study group completed six weeks of training consisting of 20 minutes of treadmill walking five days a week. The results demonstrated no significant cardiovascular improvements (as measured by maximal oxygen uptake). However, the patients did have significantly increased skeletal muscle mass measured on thigh cross-sectional area and ultrasound-estimated skeletal muscle mass (p<0.05). Additionally, there was an increase in functional ability in the KAATSU-walk training group (p<0.05). This study helped spark future research on the combination of exercise intensity and duration in conjunction with BFR.

Today, the application of BFR training for enhanced rehabilitation or modulating effects to exercise programs is gaining momentum in the sports medicine and athletic communities. A systematic review of 16 published, peer-reviewed articles, investigated current implementation methodologies in both aerobic or resistance training for well-trained athletes. The purpose was to report the musculoskeletal adaptations in different athletic populations. This systematic review included papers that used various means of BFR with pneumatic cuffs of different widths and other means of restricting flow with elastic bands. The types of exercises varied greatly with some studies of knee extension, some using squats, others including upper extremity exercises, and finally studies that used walking and running as the exercise mediums.

Five of the 16 studies as mentioned used knee extension exercises and additionally used pneumatic cuffs with documented pressures to attain partial blood flow occlusion (venous). While the studies with squat training did not reveal increased thigh girth, the knee extension studies did show both increased strength and thigh (extensor) girth in the BFR groups, especially when usual resistance training was augmented with BFR.

Several studies have demonstrated potential metabolic mechanisms for muscle hypertrophy. Manimmanakorn demonstrated increased muscle recruitment in the BFR group. Takarada et al. demonstrated venous occlusion induced hormonal growth factors and muscular hypertrophy in older female patients in the setting of low intensity resistance.
exercise. Interestingly, these findings were consistent at exercise levels far below those traditionally expected to induce skeletal muscle change.6,7,21

Most of previous study designs focus on healthy, athletic subjects. An important application of BFR training has been to treat patients in the rehabilitation phase following a period of injury or deconditioning after injury or surgical intervention. Postoperative rehabilitation can require prolonged treatment to achieve pre-injury muscular strength. Furthermore, some surgical interventions require delays in high intensity training to allow postoperative healing of repaired or reconstructed joints.6,7

In a study by Takarada et al. the effects of vascular occlusion in patients following anterior cruciate ligament reconstruction were observed. Sixteen postoperative ACL reconstruction patients were randomly assigned to an experimental or control group.9,21 Both groups participated in the same postoperative physical therapy program; however, the experimental group had 14 days of intermittent five minute intervals of venous occlusion therapy. The outcomes indicated significant decrease in postoperative extensor muscle atrophy in the experimental group (p<0.05) as demonstrated on MRI measured cross-sectional area.9

Tennett et al. conducted a pilot study of 17 postoperative arthroscopic knee patients randomized to a control or experimental group. In addition to routine postoperative physical therapy, the experimental group underwent 12 sessions of BFR exercises.8 After BFR results demonstrated a significant increase in thigh cross-sectional area at 6-cm and 16-cm proximal to the patella (P = 0.0111 and 0.0001, respectively), timed stair ascent showed greater improvements (P = 0.0281), and patient reported outcome measures significantly improved (P = 0.0149) as compared to the control group.8 Finally, the BFR group had approximately twice
the improvement in extension and flexion strength (P = 0.034) as compared to a routine physical therapy program.8

**Concerns and Risks**
Results are variable in healthy cohorts, and there are suggestions of benefit in groups utilizing knee extension in rehabilitation. The systematic review presented by Scott et al. noted no venous thrombosis, but subjects with a prior history of deep venous thrombosis and/or presence of varicosities were excluded.14 However, because many of the studies have been performed in small patient sample sizes, concern remains for possible complications associated with venous occlusion.

Although no complications have been reported, there is concern for endothelial damage and the effects on the coagulation cascade with venous stasis in the extremities. Shimizu et al. demonstrated improvements in vascular endothelial function and peripheral blood flow with significant decreases in von Willebrand factor (p<0.05).22 Tennen et al. monitored for post BFR therapy DVT before and after therapy sessions using duplex ultrasonography.8 The sample size was small, however, no vascular complications were reported.8 Madarame et al. evaluated the effects of low-intensity resistance training with BFR on the coagulation cascade in 10 patients.25 Plasma volume reduction was significantly greater after the exercise with BFR (P<0.05).25 The results suggested that in a healthy patient population, low-intensity resistance exercise with BFR does not activate the coagulation system.25

There have been rare case reports of rhabdomyolysis after BFR. The reported incidence of rhabdomyolysis after BFR is 0.008%.23 Published case reports noted an extreme rise in muscle CPK without long-term adverse complications.24 Elevated CPK was not noted in other experimental trials.21

Finally, the effect BFR training has on tendon strength and the possibility of connective tissue injuries related to increased muscle strength without concomitant tendon conditioning remains a concern.14

**Conclusion**
BFR training used as a supplement to routine resistance training could result in increased strength and muscle hypertrophy in healthy athletes. Current literature suggests that BFR while exercising at lower intensity could be used with subjects after surgery or in populations unable to perform higher levels of exertion with routine resistance training. BFR seems to provide a rehabilitation augmentation method that may have promising influences in the goal to achieve accelerated function after surgical intervention, specifically for extensor muscle atrophy.8,10,27

Overall, the utilization of venous occlusion therapy may provide patients a safe method to begin strength training at earlier stages of rehabilitation.8 However, further large-scale clinical trials need to be completed in order to obtain a better understanding of occlusion therapy physiology, complications, side effects, standardized treatment algorithms, and long-term patient outcomes.26,8,22,23
References


