

## Review

# Ischemic strength training: a low-load alternative to heavy resistance exercise?

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Strength training with low loads in combination with vascular occlusion has been proposed as an alternative to heavy resistance exercise in the rehabilitation setting, especially when high forces acting upon the musculo-skeletal system are contraindicated. Several studies on low-to-moderate intensity resistance exercise combined with cuff occlusion have demonstrated increases in muscle strength and size that are comparable to those typically seen after conventional high-load strength training. However, the physiological mechanisms by which occlusion training induces increased muscle mass and strength are currently unclear, although several

candidate stimuli have been proposed. Also, the long-term safety, practicality, and efficacy of this training method are still controversial. Furthermore, recent studies have demonstrated that in some instances, tourniquet cuffs may not be necessary for relative ischemia and significant training effects to occur with resistance exercise at low-to-moderate loads. The aims of the present review are to summarize current opinion and knowledge regarding the physiology of ischemic strength training and to discuss some of the training and health aspects of this type of exercise. In addition, suggestions for further research are given.

Strength training is an important component of training in most sports as well as in the area of injury prevention and rehabilitation (Escamilla & Wickham, 2003). In the prescription of resistance exercise, training intensity or the load used is commonly regarded as the most important variable (Fleck & Kraemer, 1997). The intensity in dynamic resistance training is often quantified as a function of the maximum weight that can be lifted only once (one repetition maximum, 1RM). Most authors agree that the load should be at least 60% of 1RM in order to stimulate increases in strength and that optimal strength gains results from loads in excess of 80% of 1RM (Atha, 1981; Häkkinen, 1994; Fleck & Kraemer, 1997; ACSM, 2002; Andersen et al., 2006). For muscle hypertrophy, loads of 6–12RM are usually recommended, corresponding to ~70–85% of 1RM (Häkkinen, 1994; Fleck & Kraemer, 1997; ACSM, 2002).

In the clinical setting, however, it is often difficult and sometimes also contraindicated to use near-maximal loads (e.g., early rehabilitation after a sports injury). Muscle atrophy and weakness often occur rapidly in the affected area due to the effects of trauma (or disease) and inactivity. Consequently,

training modalities that promote hypertrophy or counteract atrophy without the use of heavy loads should be of special interest in the rehabilitation of injuries and some chronic diseases for which high musculo-skeletal forces are contraindicated.

In the mid-1990s, Rooney et al. (1994) and Schott et al. (1995) suggested that fatigue and metabolite accumulation were important factors in the resistance exercise stimulus leading to increased strength and accretion of muscle mass. These findings were extended by Shinohara et al. (1998) and Takarada et al. (2000b), who used tourniquet cuffs to partially restrict the muscle blood flow during training with low resistance in order to cause increases in muscle strength. In these and in several subsequent studies (Takarada et al., 2002, 2004; Burgomaster et al., 2003; Abe et al., 2005a, b; Kubo et al., 2006), low-to-moderate intensity (20–50% of 1RM) resistance training with vascular occlusion has been shown to lead to gains in muscle strength and volume comparable to those seen after conventional heavy resistance training. In one recent study, hypertrophy of the quadriceps was even observed after walk training with tourniquets (Abe et al., 2006). It has also been reported that brief intermittent tourniquet-

induced ischemia-reperfusion, without exercise, can decrease disuse atrophy; at least in some muscles (Takarada et al., 2000c; Clark et al., 2006; Kubota et al., 2008).

The combination of low loads and large training effects suggests that ischemic strength training may be a useful method in rehabilitation and other contexts. However, the practicality and the safety of training with vascular occlusion remain controversial. Therefore, the purpose of the present review is to summarize current opinion and knowledge regarding the physiology of ischemic strength training and to discuss some of the training and health aspects of this type of exercise.

## **Physiology**

### **Motor unit recruitment**

It is generally believed that only muscle fibers that are activated during exercise grow as a result of strength training (Kraemer et al., 1996). The size principle of motor unit recruitment dictates that small units composed of slow but fatigue resistant fibers are recruited first and with increasing demands for force or power, increasingly larger units are recruited (Henneman et al., 1965). Studies using glycogen depletion (Gollnick et al., 1974a, b; Vøllestad et al., 1984; Vøllestad & Blom, 1985) and alterations in phosphocreatine-to-creatine ratios in muscle fibers (Beltman et al., 2004a, b) have supported the notion that the size principle is operating in humans during exercise. Thus, units with type I fibers are usually recruited first and with increasing intensity of exercise, units comprised of type IIa fibers and finally also units with type IIx fibers are recruited (Beltman et al., 2004a). In relatively large limb muscles such as the deltoid and the biceps brachii, recruitment of new motor units with increasing loads occurs up to at least 85% of maximum voluntary isometric action (MVIA) (Duchateau et al., 2006). Thus, it would appear that the heavy loads typically used in resistance training regimes are required to ensure that most motor units are recruited and thus exposed to the stimulus of strength training.

However, numerous studies (e.g., Vøllestad et al., 1984; Sahlin et al., 1997; Houtman et al., 2002, 2003) have shown that the recruitment thresholds for the motor units decrease during fatiguing exercise at submaximal loads so that type II fibers are increasingly recruited as the point of torque failure draws closer. Restricting the muscle blood flow with a tourniquet has been shown to decrease the endurance and increase the electrical activity (as measured by electromyography, EMG) of the working muscle during low-intensity exercise. For example, Takarada et al. (2000b) showed that the EMG of the biceps brachii during low-intensity resistance exercise (40%

of 1RM) combined with partial occlusion of the muscle blood flow was almost equal to that observed during conventional heavy resistance exercise (80% of 1RM). In an early study on low-intensity dynamic knee extensions performed to exhaustion during cuff occlusion, Ingemann-Hansen et al. (1981) observed glycogen depletion in both fiber types as well as low creatine phosphate levels in muscle biopsies taken immediately post exercise before the release of the occlusion. Yasuda et al. (2005) reported type II fiber hypertrophy as well as increased whole muscle cross-sectional area (CSA) after a period of low-intensity strength training (20% of 1RM) combined with vascular occlusion. Collectively, these findings strongly suggest that type II fibers are recruited also during very low-intensity ischemic training. Indeed, it has been argued that the enhanced hypertrophic response to exercise with blood flow restriction may simply be due to the recruitment of large motor units and the resulting mechanical load on the muscle fibers in these units (Meyer, 2006).

### **Response of hormones and systemic growth factors**

Heavy-resistance exercise can result in acute changes in the plasma levels of several hormones and growth factors. While some studies have also demonstrated changes in the resting levels of some hormones after short-term training, it has been argued that the acute hormonal response is of greater importance for hypertrophic adaptations than chronic changes (Kraemer & Ratamess, 2005). Hormones and systemic growth factors that have been shown to increase acutely in plasma as a result of a strength training bout include growth hormone (GH), testosterone, cortisol, insulin-like growth factor 1 (IGF-1), insulin, and catecholamines (Kraemer & Ratamess, 2005). To date, most of the research has been focused on the anabolic hormones GH and testosterone, and the catabolic hormone cortisol.

With low-load occlusion training, very large acute increases in plasma GH have been demonstrated in some studies (Takarada et al., 2000a, 2004), which led these authors to speculate that GH may play a part in the muscle hypertrophy seen after this type of training. However, the evidence for a role for GH in exercise-induced muscle hypertrophy is limited. McCall et al. (1999) reported significant correlations between the acute increases in GH and the increases in type I and type II fiber area in the biceps brachii in response to a period of strength training, but there was no relationship between increases in GH and increases in whole muscle area for the biceps brachii. Goto et al. (2005) reported significant correlations between acute exercise-induced elevations in GH and increases in quadriceps CSA after a training period. While the correlations reported in the studies of

McCall et al. (1999) and Goto et al. (2005) appear to support a role for GH, they do not prove causality. It is possible that the increased levels of GH reflected a greater level of effort, which in itself would likely be sufficient to cause increased growth. Additionally, elevated levels of GH may be caused by and/or occur in parallel to local processes which may be more important for the hypertrophic response. Furthermore, studies examining exogenous GH in combination with resistance exercise have generally not shown any significant additive effects on muscle anabolism (reviewed by Rennie, 2003). However, it should also be noted that there are several variants of GH as well as other peptides that are released from the pituitary gland in response to resistance training (Hymer et al., 2006). Thus, the physiological significance of the GH response to both conventional and ischemic strength training is currently unclear.

Many of the effects of GH are mediated by IGF-1. Originally, IGF-1 was regarded as a systemic growth factor produced by the liver under the influence of GH. During the last decades, it has become evident that GH also stimulates local IGF-1 production in the peripheral tissues, including muscle, and that GH itself has direct effects on local tissues (Goldspink et al., 2006). The acute response of circulating IGF-1 to resistance exercise is unclear (Kraemer & Ratamess, 2005). In a recent study by Popov et al. (2006), a moderate-intensity (50% of 1RM) leg press regime with no relaxation between repetitions and short inter-set rest periods (30 s) induced an acute increase in circulating IGF-1 levels, which was highly correlated with the increase in plasma GH. As will be discussed in a later section, this type of regime has many similarities with training combined with cuff occlusion.

However, it seems unlikely that an acute increase in GH could cause such immediate increases in circulating IGF-1, because the response of IGF-1 to GH pulses is delayed (3–9 h) and peak values of IGF-1 may not be reached until after 16–28 h post exercise (Kraemer & Ratamess, 2005). In a study by Goto et al. (2003a), the elevated GH levels after a combination of high and moderate-intensity resistance training were correlated with the acute increases in thigh circumference. The acute increase in muscle CSA immediately post exercise is in turn correlated with a decrease in plasma volume (Ploutz-Snyder et al., 1995). Plasma volume decreases of 20–22% have been noted after leg press and barbell squat exercises (Ploutz et al., 1993; Ploutz-Snyder et al., 1995). Therefore, the increase in IGF-1 in the study of Popov et al. (2006) may have been caused by hemoconcentration.

Furthermore, the correlation between the acute increases in GH and IGF-1 reported in the study of Popov et al. (2006) may be spurious, because of the

relationship between acute muscle volume changes and GH. The fluid shifts in resistance exercise from the circulation into the active muscles are thought to be caused largely by accumulation of lactate, hydrogen ions, sodium ions, and phosphate in the working muscles (Ploutz-Snyder et al., 1995). These metabolites and ions have also been implicated as important in the GH response to exercise, presumably through metaboreceptors in the muscles that sense changes in concentrations and provide feedback to the central nervous system (Gordon et al., 1994; Viru et al., 1998). Thus, fatiguing low-to-moderate intensity strength training during ischemic conditions leads to accumulation of metabolites and ions in the working muscles, which in turn leads to both an increase in GH secretion (through feedback from muscle metaboreceptors) and increased plasma levels of IGF-1 (mainly through hemoconcentration). Nevertheless, hemoconcentration of hormones and growth factors may be of physiological significance as increased blood concentration of these molecules, regardless of mechanism, means a greater probability of interactions with receptors (Kraemer & Ratamess, 2005).

Regarding longer term changes in resistance training with vascular occlusion, significant increases in circulating levels of IGF-1 along with gains in muscle volume were reported in one study (Abe et al., 2005a). However, it has been suggested that systemic factors may be of secondary importance in muscle hypertrophy in comparison to the “local” system of muscle adaptation (Adams, 2002; Walker et al., 2004; Eliakim et al., 2006; Goldspink et al., 2006). Still, this does not exclude the possibility that systemic factors may amplify the hypertrophy induced by the localized training, as proposed by Viru and Viru (2000). Indeed, a recent study on strength training with blood flow restriction (Madarame et al., 2008) provided evidence for a potentiating effect of systemic factors. In this study, performing additional leg exercise with vascular occlusion after arm training resulted in greater increases in both muscle area and isometric strength for the elbow flexors compared with an identical arm training regime supplemented with leg exercise without occlusion.

It is uncertain which factor(s) that could mediate this potentiating effect. In their paper, Madarame et al. (2008) suggested that noradrenaline was responsible for the enhanced hypertrophy, based on the differences in the acute response between the two regimes, while GH and testosterone did not differ significantly. They also remarked that several  $\beta$ -adrenergic agonists have anabolic effects on skeletal muscle. However, a causative role for catecholamines was not proven in their study. It should also be noted that the increase in GH was significant for the occluded regime, while the response for the

non-occluded regime was not. Hence, a role for GH, either on its own or synergistically with the catecholamine response, cannot be ruled out at present.

However, numerous studies have demonstrated marked hypertrophy in response to localized training regimes (for a review, see Wernbom et al., 2007), and Walker et al. (2004) reported equal gains in strength and muscle area in response to arm training only vs combined arm and whole-body training. From their description, it appears that the arm training routine in the study of Madarame et al. (2008) was submaximal in terms of the effort required, and the ~3–4% increase (not significant) in muscle area in the trained arm in the non-occluded group compared with the ~11–12% increase in the occluded group suggests that it was largely unsuccessful in itself. Therefore, it is presently unclear whether an additive effect of an enhanced systemic response would occur in the presence of a more effective local training stimulus. Furthermore, while the amplifying effect was present in the trained arm, the untrained arm did not increase in muscle area (~1%). Thus, as the authors themselves noted, a local exercise stimulus is indispensable for muscle hypertrophy.

#### Local growth factors and intracellular signaling pathways

It is generally held that significant hypertrophy is seen only in the exercised muscle and not in the other muscles in the body (Adams, 2002; Goldspink et al., 2006). Several mechanisms intrinsic to the muscle are involved in the localized hypertrophic response to resistance training, including autocrine/paracrine growth factors, intracellular signaling induced by changes in the local environment (e.g., transduction of mechanical tension into intracellular signals), and changes in the content of receptors of hormones and growth factors.

IGF-1 is expressed in skeletal muscle in addition to being present in the circulation, which means that it can also act as a local growth factor. Changing the availability of the muscle growth factors IGF-1 and mechano-growth factor (MGF, a splice variant of IGF-1) and myostatin appears to be a central regulatory process in adaptive skeletal muscle growth (Rennie et al., 2004). Localized infusion of IGF-1 or MGF as well as genetic overexpression of IGF-1 has been shown to increase muscle mass (reviewed by Goldspink et al., 2006) and increases in IGF-1 variants in skeletal muscle have been demonstrated in several animal and human models of functional overload, including resistance exercise (reviewed by Rennie et al., 2004; Glass, 2005; Tidball, 2005). Hypertrophic intracellular signaling downstream of IGF-1 include the phosphatidylinositol-3 kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) and the PI3K/Akt/glycogen synthase kinase

3 $\beta$  (GSK3 $\beta$ ) pathways (Rennie et al., 2004; Glass, 2005; Tidball, 2005). Akt is also known as protein kinase B (PKB). The downstream targets of the PI3K/Akt/mTOR pathway are the translational regulators p70S6 kinase (p70S6K) and eukaryotic initiation factor-4E-binding protein (4E-BP) (Adams, 2002; Rennie et al., 2004; Glass, 2005). Downstream in the PI3K/Akt/GSK3 $\beta$  pathway is the eukaryotic initiation factor 2B (eIF2B). The end results of activation of these pathways are increases in protein synthesis and cell growth (Bolster et al., 2004; Glass, 2005; Baar et al., 2006).

Contrary to the anabolic effects of IGF-1/MGF on skeletal muscle, myostatin acts as a negative regulator of skeletal muscle growth (Roth & Walsh, 2004). Increases in IGF-1/MGF have been observed after acute bouts and longer term strength training (reviewed by Goldspink et al., 2006, see also Kim et al., 2005; Petrella et al., 2006). Reductions in myostatin have been noted in several (Roth et al., 2003; Walker et al., 2004; Kim et al., 2005; Petrella et al., 2006; Raue et al., 2006; Hulmi et al., 2007) but not all (e.g., Willoughby, 2004) studies on the myostatin response to strength training. Based on these observations, it has been hypothesized that the up-regulation of IGF-1/MGF and the downregulation of myostatin are necessary for an optimal hypertrophic response (Kim et al., 2005).

Regarding any possible effects of occlusion training on local IGF-1/MGF in humans, there are at present no data available. There are also currently no reports concerning changes in myostatin in humans in conjunction with ischemic strength training. In a rat model of partial vascular occlusion, myostatin levels were shown to decrease along with increases in muscle weight and myofiber areas (Kawada & Ishii, 2005). Interestingly, no significant increase in the expression of IGF-1 was seen in this model. However, it should be noted that the model used by Kawada and Ishii (2005) involved chronic restriction of blood flow, as opposed to the intermittent occlusion models used in human studies and that this difference may result in substantially different adaptations.

The tension developed by the muscle appears to be a critical stimulus for the hypertrophy associated with strength training. Apart from acting via the induction of local growth factors such as IGF-1/MGF, it is becoming increasingly evident that mechanical tension can directly activate anabolic signaling pathways (reviewed by Vandeburgh, 1992; Hornberger & Esser, 2004; Huijling & Jaspers, 2005). It has been noted that the earliest activation of hypertrophic signaling after resistance exercise is too rapid to be accounted for by growth factors. Consequently, the involvement of mechanochemical transduction, and/or other processes such as calcium

release, have been suggested in this early response, which is followed by a late response presumably involving growth factors such as IGF-1/MGF (Wackerhage & Rennie, 2003). Recently, it was observed that a functional IGF-1 receptor is not necessary for overload-induced muscle hypertrophy in rats (Spangenburg et al., 2008); a finding which strengthens the case for the importance of direct mechanotransduction. It is beyond the scope of this paper to discuss the possible mechanisms by which tension is transduced into intracellular signals; the interested reader is referred to the reviews above and to recent original papers (Boppart et al., 2006; Hornberger et al., 2006; Spangenburg & McBride, 2006). Interestingly, there appears to be some overlap between the pathways activated by mechanical stimuli and those activated by growth factors (Tidball, 2005).

In a recent study (Fujita et al., 2007), an acute bout of low-intensity (20% of 1RM) resistance training combined with vascular occlusion increased muscle protein synthesis, along with an increase in the phosphorylation of p70S6K and a decreased phosphorylation of eukaryotic elongation factor 2 (eEF2). These authors concluded that hormonal changes, metabolic stress, and/or mechanotransduction signaling might have been involved in the mTOR/p70S6K signaling. Because post exercise biopsies were obtained only at a time point of 3 h after exercise, and no data on growth factor responses were reported, it is difficult to assess the relative contributions of growth factors vs mechanotransduction and/or other early events, including systemic responses, with this type of training.

#### Other exercise-related factors

Apart from hormones, growth factors and mechanical stimuli, a wealth of other factors in the environment of the muscle also affect intracellular signaling. Changes in blood flow (Kraemer & Ratamess, 2004), heat stress (Goto et al., 2003), reactive oxygen species (ROS) (Takarada et al., 2000a), hypoxia–hyperoxia (Kawada, 2005), and nitric oxide (NO) (Kawada & Ishii, 2005) have all been suggested as possible stimuli in training with vascular occlusion.

Blocking endogenous NO production decreases the hypertrophic response by ~50% in animal models of functional overload (Smith et al., 2002; Sellman et al., 2006). Furthermore, it has been demonstrated that satellite cells can be activated in response to mechanical stretch by the release of hepatocyte growth factor (HGF) in a NO-dependent manner (Tatsumi et al., 2006). In addition, NO is involved in other mechanotransduction processes such as integrin signaling (Zhang et al., 2007). The isoforms of nitric oxide synthase (NOS) are activated

by numerous stimuli, including exercise and possibly also hypoxia (Stamler & Meissner, 2001).

In their study on a rat model of chronic partial occlusion, Kawada and Ishii (2005) reported increased levels of NOS-1 mRNA along with the increase in muscle weight. However, changes in other possible regulators of muscle mass were also present, such as a decrease in myostatin and an increase in heat shock protein 72 (HSP-72). Little is currently known regarding the possible roles of NO in muscle hypertrophy in human models of resistance training, including ischemic strength training.

It has been suggested that NO regulates the expression of cyclooxygenase 2 (COX-2) in skeletal muscle (Soltow et al., 2006). The COX enzymes catalyze the production of prostaglandins from arachidonic acid that is released from membrane phospholipids by the enzyme phospholipase A<sub>2</sub> (Bos et al., 2004; Shen et al., 2006). Prostaglandins of the COX-2 pathway include prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and prostaglandin F<sub>2</sub> α (PGF<sub>2α</sub>). These were implicated in mechanotransduction and the control of protein synthesis and degradation already in the early 1980s (for a review see Thompson & Palmer, 1998). Blocking the production of these prostaglandins blunts the increased protein synthesis after an acute bout of heavy eccentric exercise (Trappe et al., 2001, 2002). Furthermore, recent data suggest that the COX-2 pathway is important for myonuclear addition *in vivo* and satellite cell activation and proliferation *in vitro* (Bondesen et al., 2006), and PGF<sub>2α</sub> may regulate hypertrophy of skeletal muscle by activating both cell fusion and protein synthesis (Horsley & Pavlath, 2003).

To date, no training study in humans has been published which has confirmed the role of prostaglandins in skeletal muscle hypertrophy, but experiments with rodent models have demonstrated the importance of the COX-2 pathway in recovery from atrophy (Bondesen et al., 2006) and for hypertrophy resulting from functional overload (Soltow et al., 2006). Also, a recent human study has shown increased levels of PGF<sub>2α</sub> after conventional resistance exercise (Trappe et al., 2006).

Whether prostaglandins are produced in humans also in response to low-load training with vascular occlusion is currently not known. However, increased muscle levels of arachidonic acid and prostaglandins have been noted in studies on cats subjected to electrically induced isometric exercise and ischemia, and greater increases were seen after a combination than after either intervention alone (Rotto et al., 1989; Symons et al., 1991). Moreover, prostaglandins are involved in the sensitization and stimulation of group III and IV muscle afferents, and the responses of these afferents are increased during dynamic exercise with occlusion compared with

freely perfused conditions (Hayes et al., 2006). Group IV thin fibers represent the afferent pathway from metaboreceptors and may mediate the GH response during muscle activity (Virus et al., 1998). On the basis of these observations, we suggest that the potential role of prostaglandins in ischemic strength training should be investigated.

Regarding the potential role of ROS in muscle hypertrophy, several interesting observations have been made in both skeletal muscle and cardiac muscle. ROS have been implicated in cardiac hypertrophy; an effect which may be mediated via phosphatidic acid, which in turn is regulated by the enzyme phospholipase D (Tappia et al., 2006). In skeletal muscle, recent evidence strongly suggests a role for phospholipase D activation and subsequent production of phosphatidic acid in mTOR signaling in response to mechanical stimulation (Hornberger et al., 2006). In cardiac muscle, activation of phospholipase D is seen in the early part of the reperfusion after ischemia, whereas following prolonged reperfusion, a reduced activity is seen instead (Tappia et al., 2006). These authors speculated that low levels and brief exposures to ROS may stimulate phospholipase D-mediated signal transduction, whereas prolonged exposure and high levels of ROS result in phospholipase D inhibition. In line with these observations, low levels of hydrogen peroxide ( $H_2O_2$ ) induces hypertrophy in cardiac myocytes, whereas higher concentrations result in apoptosis (Kwon et al., 2003).

Concerning skeletal muscle, growing evidence supports a role for ROS in muscle atrophy (reviewed by Powers et al., 2007), but again, this can possibly be explained by the negative effects of prolonged exposures and high levels of ROS, as opposed to brief exposures to low concentrations of ROS. Furthermore,  $H_2O_2$  induces activation of p70S6K in different cell types (Bae et al., 1999; Tu et al., 2002), and it has been suggested that  $H_2O_2$  acts as a second messenger in growth factor-induced p70S6K signaling (Bae et al., 1999). Given these findings, we suggest further studies on the possible involvement of ROS in mediating some of the hypertrophic adaptations to strength training during the ischemic conditions.

As argued by Widegren et al. (2001), it is unlikely that exercise responses are caused by one single mechanism and more likely that they depend on the integration of multiple local and systemic factors. As is obvious from the above discussion, numerous mechanisms may contribute to the hypertrophic effects seen after ischemic strength training. Current evidence suggests that the high degree of motor unit recruitment is a major factor, and there is also some data indicating that the systemic response may enhance the effects of the mechanical tension during certain circumstances (e.g., at low-to-moderate

loads). The evidence for additive and/or independent effects of ischemia–reperfusion in the training situation, although an attractive hypothesis, is limited. Further investigations are obviously needed to study both the impact of individual factors and the interplay between them.

### **Practical and health aspects**

#### **Is occlusion training safe and feasible?**

As discussed by Takarada et al. (2000b), training with cuff occlusion may have the potential to create muscle damage and other serious side effects such as thrombosis and damage to blood vessels. Furthermore, high levels of ROS are linked to proteolysis and apoptosis (Powers et al., 2007). However, in another study by Takarada et al. (2000a), no evidence of muscle damage or high levels of oxidative stress were found as judged by the low levels of creatine kinase and lipid peroxide after their protocol. Although measurements of fiber areas have been included in a few studies (Ohta et al., 2003; Yasuda et al., 2005), little is currently known about the effects of occlusion training on soft tissues beneath and distal to the tourniquet, including markers of proteolysis, apoptosis, and necrosis.

In our literature search, we found 13 training studies (see Table 1 for references) using blood flow restriction with a tourniquet. These studies on occlusion training have typically lasted between 2 and 8 weeks, but two studies (Takarada et al., 2000b; Ohta et al., 2003) lasted for 16 weeks. In these 13 studies, a total of 116 subjects trained a total of 4376 training sessions. In most of them, the occlusion was partial and the duration of occlusion generally lasted between 5 and 10 min and except for acute muscle pain, no adverse effects were reported. In a study by Kilian et al. (2005), 10 min of complete occlusion of the forearm resulted in no measurable effects on leukocyte and platelet activation and even 20 min of ischemia failed to result in measurable changes. Although some endothelial dysfunction was noted with especially the longer duration, this was essentially recovered within 60 min.

Recently, Nakajima et al. (2006) published a survey on the safety of occlusion training based on reports from 105 training centers in Japan, where this method, also termed “Kaatsu training”, has become widely popular for both fitness and rehabilitation purposes. A total of over 12 600 individuals had trained using tourniquets in combination with different modes of exercise (walking, cycling, weight training, etc.). The most common side effects were subcutaneous hemorrhage (incidence: 13.1%) and temporary numbness (1.3%). More serious side effects were rare: venous thrombosis (0.055%), deterioration of ischemic heart disease (0.016%), cerebral

**Table 1. Studies examining training effects of resistance exercise combined with vascular occlusion**

Reference	Gender, Age (no of subjects)	Training status	Training methods	Exercise(s)	Intensity (% of 1RM)	Sets	Reps	Rest between sets (s)	Frequency (sessions/week)	Period length (days)	Change in muscle strength (%)	Change in muscle size (% CSA)	% change per day (method)	Comments	
Shinohara et al. (1998)	Males (5) 23 (19–29)	Untrained	Isometric (+vascular occlusion)	Knee extension (unilateral)	40 of MVC	1	~ 36		3	28	+26 (MVC)	–	–	Continuous severe occlusion, >250 mmHg, cuff width not reported. Intermittent exercise, 2 s duration with 3 s rest in between.	
Takarada et al. (2000b)	Females (11) 58 ± 2	Untrained	Isometric	Knee extension (unilateral)	40 of MVC	1	~ 36		3	28	+9 (MVC)	–	–	Contralateral leg, which was trained as above but without occlusion.	
			Conc+Ecc weight resistance (+VO)	Elbow flexion (unilateral)	53	3	~ 18	60		2	112	+18.4 (average of torques, –90 to 90°/s)	+20.3 (biceps) +17.8 (brachialis)	+0.22 (MRI)	Continuous partial occlusion. Cuff width = 33 mm, cuff pressure ~ 110 mmHg. Training to failure in each set.
			Conc+Ecc (WR)	Elbow flexion (unilateral)	76	3	~ 19	60		2	112	+22.6 (–90 to 90°/s)	+18.4 (biceps) +11.8 (brachialis)	+0.18	Contralateral arm trained at high intensity without occlusion. Training to failure in each set.
Takarada et al. (2002)	Females (8) 57 ± 2	Untrained	Conc+Ecc (WR)	Elbow flexion (unilateral)	54	3	~ 18	60		2	112	+1.0 (–90 to 90°/s)	+6.9 (biceps) +3.8 (brachialis)	+0.06 (MRI)	Group that trained at the same relative intensity and volume but without occlusion.
			Conc+Ecc (WR+VO)	Knee extension (bilateral)	50	5	~ 16	30		2	56	+14.3 (0–180°/s)	+12.3 (biceps) +3.8 (quadriceps)	+0.03	Continuous partial occlusion. Cuff width = 33 mm, cuff pressure ~ 196 mmHg. Training to failure in each set.
			Conc+Ecc (WR)	Knee extension (bilateral)	50	5	~ 16	30		2	56	+3.2 (0–180°/s)	–	–	Group that trained at the same relative intensity and volume but without occlusion.
Burgomaster et al. (2003), Moore et al. (2004)	Males (5) 26 ± 1	Strength-trained rugby players	Conc+Ecc (WR)	Elbow flexion (unilateral)	~ 50	3–6	~ 5–10	60		2	56	+10.5 (concentric torque 60°/s) +23 (1RM) +10 (MVC)	–	–	Continuous partial occlusion. Cuff width = 70 mm, cuff pressure ~ 100 mmHg. Five minutes rest between set 3 and 4. Training to failure in most of the sets.
			Conc+Ecc (WR)	Elbow flexion (unilateral)	~ 50	3–6	~ 5–10	60		2	56	+9.6 (concentric torque 60°/s) +23 (1RM) +0 (MVC)	–	–	Contralateral arm, which was trained without occlusion. Number of repetitions was matched to that of the occluded arm.
			Conc+Ecc (WR+VO)	Knee extension (bilateral)	16–22	5	15–23	60		2	56	+9.2 (average of torques, 0–180°/s)	+10.3	+0.18 (MRI)	Continuous partial occlusion. Cuff width = 90 mm, cuff pressure ~ 218 mmHg. Training to failure in each set.
Abe et al. (2005a)	Males (6) 24 ± 8	Physically active	Conc+Ecc (WR)	Knee extension (bilateral)	16–22	5	15–23	60		2	56	+3.1 (average of torques, 0–180°/s) +16.8 (1RM)	+1	+0.02 (MRI)	Group that trained at the same relative intensity but without occlusion.
			Conc+Ecc (WR+VO)	Squat (machine)	20	3	15	30		12 (6 days, 2 × /d)	+8.0 (quadriceps) +8.0 (adductors) +9.1 (gluteus maximus) +10.7% (hamstrings) +1.8 (quadriceps) +0.2 (adductors) +1.4 (gluteus)	+8.0 (quadriceps) +8.0 (adductors) +9.1 (gluteus maximus) +10.7% (hamstrings) +1.8 (quadriceps) +0.2 (adductors) +1.4 (gluteus)	+0.57 (MRI)	Continuous partial occlusion. Narrow cuff, width not reported. Pressure increased from ~ 160 to 240 mmHg during the training period.	
			Conc+Ecc (WR+VO)	Knee flexion	20	3	15	30		12 (6 days, 2 × /d)	+22.6 (1RM)	+22.6 (1RM)	+0.76 (MRI)	Group that trained at the same relative intensity but without occlusion.	
Takarada et al. (2004)	Males (6) 21 ± 1	Physically active	Conc+Ecc (WR+VO)	Knee extension (bilateral)	16–22	5	15–23	60		2	56	+9.2 (average of torques, 0–180°/s)	+10.3	+0.18 (MRI)	Continuous partial occlusion. Cuff width = 90 mm, cuff pressure ~ 218 mmHg. Training to failure in each set.
			Conc+Ecc (WR)	Knee extension (bilateral)	16–22	5	15–23	60		2	56	+3.1 (average of torques, 0–180°/s) +16.8 (1RM)	+1	+0.02 (MRI)	Group that trained at the same relative intensity but without occlusion.
Abe et al. (2005a)	Males (7) 24 ± 8	Physically active	Conc+Ecc (WR)	Squat (machine)	20	3	15	30		12 (6 days, 2 × /d)	+8.9 (1RM)	+1.8 (quadriceps) +0.2 (adductors) +1.4 (gluteus)	+0.57 (MRI)	Continuous partial occlusion. Narrow cuff, width not reported. Pressure increased from ~ 160 to 240 mmHg during the training period.	
			Conc+Ecc (WR)	Squat (machine)	20	3	15	30		12 (6 days, 2 × /d)	+8.9 (1RM)	+1.8 (quadriceps) +0.2 (adductors) +1.4 (gluteus)	+0.57 (MRI)	Continuous partial occlusion. Narrow cuff, width not reported. Pressure increased from ~ 160 to 240 mmHg during the training period.	

Table 1. (continued)

Reference	Gender, Age (no of subjects)	Training status	Training methods	Exercise(s)	Intensity (% of 1RM)	Sets	Reps	Rest between sets (s)	Frequency/Period (sessions/ week) (days)	Change in muscle strength (%)	Change in muscle size (% CSA)	% change per day (method)	Comments	
Abe et al. (2005b)	Males (9)	Track and field athletes	Conc+Ecc (WR)	Knee flexion	20	3	15	30	12 (6 days, 14 2 × /d)	+1.3 (1RM)	+1.5% (hamstrings)	+0.11 (MRI)		
				Squat (machine)	20	3	15	30	14 (7 days, 8 2 × /d)	+9.6 (1RM)	+5.9 (quadriceps thickness)	+0.74 (UL)	Continuous partial occlusion. Narrow cuff, width not reported.	
				Knee flexion	20	3	15	30	14 (7 days, 8 2 × /d)	–	+4.5% (hamstrings thickness)	+0.56 (UL)	Pressure increased from ~ 160 to 240 mmHg during the training period.	
Males (6)	Track and field athletes	Conc+Ecc (WR)	Squat (machine)	20	3	15	30	14 (7 days, 8 2 × /d)	+4.8 (1RM)	± 0 (quadriceps thickness)	± 0 (UL)	Group that trained at same relative intensity but without occlusion.		
			Knee flexion	20	3	15	30	14 (7 days, 8 2 × /d)	–	± 0 (hamstrings thickness)	± 0 (UL)			
			Knee extension (unilateral)	20	4	12–25	30	3	84	+7.8 (MVC)	+5.9 (quadriceps volume)	+0.07 (MRI)	Continuous partial occlusion. Narrow cuff, width not reported. Cuff pressure increased from ~ 180 to 240 mmHg during the training period.	
Kubo et al. (2006)	Males (9)	–	Conc+Ecc (WR)	Knee extension (unilateral)	80	4	10	60	3	84	+7.4 (quadriceps volume)	+0.09 (MRI)	Contralateral leg, which was trained without occlusion and at heavier loads.	
				Knee extension (bilateral)	30	3	15–30	30	2	70	+19.6 (MVC)	+4.3 (quadriceps)	+0.06 (MRI)	Continuous partial occlusion. Cuff width = 40 mm. Cuff pressure increased from ~ 160 to 240 mmHg during the training period.
				Knee flexion (bilateral)	30	3	15–30	30	2	70	+18.3 (MVC)	+5.7% (hamstrings)	+0.08 (MRI)	Arm was trained without vascular occlusion.
Madarambe et al. (2008)	Males (8)	Untrained	Conc+Ecc (WR)	Elbow flexion (unilateral)	50	3	10	180	2	70	+11.5% (elbow flexors)	+0.16 (MRI)	Group that trained without occlusion.	
				Knee extension (bilateral)	30	3	15–30	30	2	70	+4.6 (MVC)	–1.3 (quadriceps)	–0.02 (MRI)	
				Knee flexion (bilateral)	30	3	15–30	30	2	70	+2.9 (MVC)	+0.3% (hamstrings)	+0.00 (MRI)	
Laurentino et al. (2008)	Males (8)	Physically active	Conc+Ecc (WR)	Elbow flexion (unilateral)	50	3	10	180	2	70	+3.5% (elbow flexors)	+0.05 (MRI)	Arm was trained without vascular occlusion.	
				Knee extension (unilateral)	~ 80	3–4	6	120	2	56	+34.5 (1RM)	+5.0 (quadriceps)	+0.09 (MRI)	Intermittent occlusion. Cuff width = 140 mm. Cuff pressure = 126 mmHg. Training to failure in each set.
				Knee extension (unilateral)	~ 80	3–4	6	120	2	56	+36.9 (1RM)	+6.1 (quadriceps)	+0.11 (MRI)	Contralateral leg, which was trained without occlusion. Training to failure in each set.
Males (8)	Physically active	Conc+Ecc (WR)	Knee extension (bilateral)	~ 60	3–4	12	120	2	56	+35.3 (1RM)	+4.5 (quadriceps)	+0.08 (MRI)	Intermittent occlusion. Cuff width = 140 mm. Cuff pressure = 131 mmHg. Training to failure in each set.	
			Knee extension (unilateral)	~ 60	3–4	12	120	2	56	+37.6 (1RM)	+3.2 (quadriceps)	+0.06 (MRI)	Contralateral leg, which was trained without occlusion. Training to failure in each set.	

The studies of Ohta et al. (2003), Ishii et al. (2005) and Teramoto and Golding (2006) are not included in this table, because it was not possible to quantify the exercise intensities in relative terms from the descriptions of their training programs. The study of Yasuda et al. (2005) was based on subjects from the study of Abe et al. (2005a) and is therefore not included in this table. 1RM, one repetition maximum; Con, concentric; CSA, cross-sectional area; Ecc, eccentric; MRI, magnetic resonance imaging; MVC, maximal voluntary (isometric) contraction; Reps, repetitions; UL, ultrasound; VO, vascular occlusion; WR, weight-based resistance.

infarction (0.008%), rhabdomyolysis (0.008%), and pulmonary embolism (0.008%). It should be noted that this report was published by the same research group that has conducted most of the studies on this type of training. In summary, although current evidence suggests it may be a relatively safe mode of training in the short term, more research is needed regarding potential adverse effects and how these can be minimized.

Apart from safety issues, the muscle pain experienced during ischemic strength training can be intense, and delayed onset muscle soreness (DOMS) is not uncommon (Wernbom et al., 2006). The DOMS subsides after a few workouts, suggesting a repeated bout effect, and it also appears that if the initial volume is low (e.g., 1–2 sets), much of the DOMS can be avoided (unpublished observations). Still, training combined with ischemia clearly requires a high degree of motivation from the trainee, especially if performed with a high level of effort.

#### Narrow or wide tourniquets?

A question which is of both practical and physiological relevance for training with pressure cuffs is the width of the tourniquet. In the context of limb surgery, it has been recommended that wide tourniquets should be used, as wide cuffs have been shown to achieve occlusion at considerably lower pressures than more narrow cuffs (Crenshaw et al., 1988; Graham et al., 1993). With wide tourniquets and lower pressures, the deleterious effects of high compression and shear forces on soft tissues may be reduced (Crenshaw et al., 1988; Graham et al., 1993).

In most of the training studies published up to date, narrow cuffs have been used at pressures of between 160 and 240 mmHg. Takano et al. (2005) used a pressure of 160–180 mmHg in combination with a 33 mm pressure belt and showed a reduction in femoral blood flow to about 30% of normal resting conditions, before exercise. Immediately after exercise, the blood flow was still markedly reduced to about 50% of that measured during rest. With a 140-mm-wide cuff, Laurentino et al. (2008) reported cessation of the tibial artery pulse (measured with Doppler) at pressures of  $\sim 130$  mmHg. Using a 135-mm-wide curved tourniquet with a 100-mm-wide-pneumatic bag inside it, we have found that pressures of  $\sim 90$ –110 mmHg are usually sufficient to partially restrict blood flow and affect muscle endurance (unpublished observations). Thus, it appears that high pressures during training are not necessary with wide tourniquets and should probably be avoided because of potential risks with the combination of severe occlusion and a high degree of compression.

An obvious drawback with wide pressure cuffs is that they may interfere with the exercise, but this is probably more significant when training the upper limb than the lower limb. However, the upper limb requires less pressure to achieve occlusion and therefore the tourniquets can be somewhat narrower. Even so, relatively wide cuffs of 70–90 mm in width and relatively low pressures (100 mmHg) have been applied in some experiments on occlusion training for the elbow flexors (Takarada et al., 2000b; Moore et al., 2004). Another potential drawback with wide cuffs is that more tissue gets compressed, but this is likely more than outweighed by the reduction in shear forces and pressure gradients. Also, the inter-individual variability in the pressure needed to achieve complete occlusion is considerably smaller with wide cuffs because the occlusion effect with these is much less dependent on the circumference of the limb (Crenshaw et al., 1988). Translated to the training situation, this should make it easier to find a proper pressure to achieve a partial occlusion. Taken together, it appears that relatively wide cuffs are preferable to narrow cuffs.

#### Are tourniquets necessary to induce relative ischemia with low-load training?

Studies investigating the static endurance of various muscle groups have shown that the difference in endurance between conditions of cuff occlusion and no occlusion disappears when the force level reaches  $\sim 40$ –60% of maximal voluntary isometric action (MVIA), (Bonde-Petersen et al., 1975; Hisaeda et al., 2001). This can be explained by the intramuscular occlusion of the blood flow which occurs due to the high pressure in the muscle (Sadamoto et al., 1983; Sejerstedt et al., 1984; Sjøgaard et al., 1988). Until recently, little data existed about the effects of cuff occlusion on endurance during conventional dynamic resistance training. Using a wide tourniquet and a pressure of 200 mmHg during the dynamic knee extension exercise with coupled concentric–eccentric actions, Wernbom et al. (2006) demonstrated significant differences in the number of repetitions performed between occluded and non-occluded conditions for loads of 20–40% of 1RM, but not for 50% of 1RM, when the exercise was performed continuously with no relaxation of the quadriceps. Thus, similarly to continuous isometric exercise, the application of a pressure cuff around the thigh appears to reduce knee extension endurance at low loads but not at moderate and heavier loads.

However, although the tourniquet affected the endurance at 20–40% of 1RM, these differences were minor at 30% and especially 40%. Furthermore, the subjects experienced ischemic pain in the working quadriceps even without a pressure cuff and

at loads as low as 20% of 1RM. In support of these findings, Shoemaker et al. (1994) noted that the blood flow to the quadriceps was inadequate during continuous dynamic knee extension exercise at a load as low as 10% of MVIA. Further evidence that intramuscular restriction of blood flow can occur at low intensities was provided by de Ruiter et al. (2007), who showed that the oxygenation level in the vastus lateralis and medialis during isometric knee extensions reached values similar to total cuff occlusion already at torques of  $\sim 25\%$  of MVIA.

Muscle blood flow mainly occurs in the relaxation period between muscle actions (Bangsbo & Hellsten, 1998). Therefore, the dynamic knee extension, preferably in a cam-type machine with variable resistance, can be used to induce relative ischemia already at loads of  $\sim 20\text{--}30\%$  of 1RM if performed in a non-stop manner to fatigue and with short rest periods (e.g., 15–45 s) between sets. Other quadriceps exercises can also be modified to achieve intramuscular restriction of blood flow. During closed kinetic chain exercises such as the squat and the leg press, the force demands of the movement dictate that the electrical activity of the quadriceps is high at flexed knee angles ( $90^\circ\text{--}100^\circ$ ) and low near full-knee extension (Andersen et al., 2006). If the range of motion instead is limited to between  $\sim 50^\circ$  and  $100^\circ$  of flexion, the muscle activity remains fairly high throughout the movement and intramuscular occlusion is thus more likely to occur.

Several studies (Takarada & Ishii, 2002; Tanimoto & Ishii, 2006; Popov et al., 2006) have demonstrated muscle hypertrophy in the quadriceps as a result of conventional training with high work/rest ratios at intensities of  $\sim 50\%$  of 1RM. Also, Laurentino et al. (2008) did not find any enhanced strength and hypertrophy in the quadriceps when cuff occlusion was added at training loads of  $\sim 60\%$  and  $\sim 80\%$  of 1RM. In our laboratories, we have noted high levels of muscle activity even without tourniquets at loads as low as 20–30% of 1RM in some exercises such as dynamic knee extensions, with the no-relaxation technique performed all-out to fatigue (manuscript in preparation). We therefore speculate that hypertrophy is possible without pressure cuffs even at these low intensities. In this context, it is noteworthy that in the occlusion training studies published to date, the groups that have trained without tourniquets have generally not trained to failure, whereas the occlusion groups have.

Intuitively, a training model which is based on the muscles own internal restriction of blood flow would have advantages both from a safety point of view and from a practical point of view. On the other hand, in certain muscle groups and in some individuals, it may be difficult to induce relative ischemia at low loads by exercise alone, due to factors such as

insufficient intramuscular pressures developed during exercise. Furthermore, it is possible that there are differences between the muscle ischemia resulting from exercise alone and the ischemia induced with a tourniquet in combination with exercise (e.g., a greater build-up of metabolites in the cuff-occluded muscle), which in turn could lead to differences in the stimulation of hypertrophic pathways. Future studies should compare the effects of ischemic training with and without cuff occlusion at the same level of effort.

### Dose–response aspects of ischemic training

A strength training program can be described by a number of variables, the most important being frequency, intensity, volume, and mode of training. Conventional heavy resistance training for the purpose of gaining muscle mass is usually performed for two to three sessions per week per muscle group, and most rehabilitation programs aiming to restore muscle volume use similar training frequencies. A recent review (Wernbom et al., 2007) suggested that the average rate of gain for the quadriceps as a result of strength training for two to three sessions per week is in the order of  $\sim 0.11\%$  increase in CSA per day. In the study of Abe et al. (2005a), in which unusually rapid gains were noted ( $\sim 0.57\%$  increase per day on average), training was performed for two sessions per day, 6 days per week for a total of 12 sessions per week. This may seem like an extremely high frequency, but the authors speculated that because of the low mechanical stress (20% of 1RM) and little muscle damage, a much shorter recovery time between sessions was needed in comparison to conventional strength training. Although the training included three sets of 15 repetitions, it is likely that the first two sets served to accumulate fatigue and that only the final set of each exercise was performed with a high level of effort. However, the training period was very short (2 weeks) and the gains were markedly slower during the second week than the first. It is therefore uncertain whether this frequency can be effective for longer periods or if overtraining would occur. From an adherence point of view, such a high frequency is unrealistic for most people.

Normal frequencies (two to three times per week) have also been used with marked hypertrophy of the quadriceps as a result (Takarada et al., 2002, 2004; Kubo et al., 2006; Madarame et al., 2008). The rates of hypertrophy observed in these four studies were between 0.04% and 0.22%/day (Table 1), which is within the range reported for conventional heavy resistance training (0.03–0.26%/day) at similar frequencies (reviewed by Wernbom et al., 2007). However, in these studies, multiple sets to failure or near were used. It is currently unknown if multiple sets of

fatiguing ischemic training is productive at higher frequencies than two to three sessions per week. Equally unknown is whether low-intensity ischemic strength training in which only the final set is performed with a high degree of effort can induce hypertrophy when performed for two to three sessions per week. At present, the interactions between frequency, intensity, and volume in ischemic strength training are not well understood.

Not all modes of ischemic training are associated with increases in muscle strength and/or marked increases in muscle protein content. Eiken et al. (1991) investigated the effects of partial occlusion in a one-leg endurance cycling model and demonstrated an 8% decrease in maximum peak torque after 4 weeks of training, four times per week for 45 min per session. This occurred in spite of increased muscle fiber CSAs of both type I and type II fibers in the ischemic leg in comparison with the normally trained leg. The authors speculated that the decreased maximum strength in the ischemic leg was due to an increased proportion of type I fibers that was evident in this leg after the training period compared with the normal leg, suggesting that a fiber type shift had occurred. In a later study from the same research group, increases in both mean fiber area (12%) and quadriceps muscle CSA (5%) were noted along with increased glycogen content in the ischemically trained muscles (Nygren et al., 2000). These authors then went on to investigate the effect of glycogen loading on muscle CSA and found that quadriceps muscle CSA increased by 3.5% when the subjects went from a glycogen depleted state to a loaded state during the course of 4 days (Nygren et al., 2001). These authors concluded that glycogen loading might contribute to the increase in muscle CSA seen after ischemic training. It should be noted that the increase in glycogen content as a result of glycogen loading from a depleted state was  $\sim 1.7$  times larger than the increase seen after ischemic cycling.

Taken together, it appears that ischemic endurance cycling, as performed in the studies of Eiken, Nygren and colleagues, leads to only minor increases in contractile protein content in the trained muscles. Interestingly, similar increases in glycogen content have been noted after ischemic strength training (Burgomaster et al., 2003). However, because significant strength gains are usually reported and because several studies have demonstrated gains in muscle CSA that have been substantially larger than  $\sim 3\%$ , the contribution of increases in glycogen content to the hypertrophy seen after this type of training is probably minor.

It is not immediately obvious why walk training with tourniquets (Abe et al., 2006) seems to be a better mode for inducing increases in both muscle strength and size than ischemic endurance cycling.

Hypertrophy training is generally short lasting and on the strength/power side of the strength-endurance continuum (Nader, 2006). Accordingly, it is possible that performing ischemic training in short intermittent working sets may cause the exercise-induced signaling to be more directed toward hypertrophic adaptations compared with longer continuous bouts. Also, longer ischemic bouts are associated with marked increases in plasma cortisol (Virus et al., 1998), which potentially cancel out some of the anabolic effects of the exercise. Differences in training frequency and/or the degree and pattern of ischemia-reperfusion may also contribute to the different results for walk training with tourniquets compared with ischemic cycle training.

### Low-to-moderate load ischemic training as an addition to heavy resistance exercise

In a series of studies, the group of Takamatsu and colleagues investigated the effects of adding fatiguing low-to-moderate intensity sets after high-intensity sets on adaptations in muscle strength and size as well as on acute hormonal responses (Choi et al., 1998; Masuda et al., 1999; Goto et al., 2003a, b, 2004). Choi et al. (1998) demonstrated a high rate of increase in quadriceps muscle area after a regime where high-intensity sets (70–80% of 1RM) were followed by sets to fatigue at succeeding lower loads (50–60% and 40–50% of 1RM), with 30 s rest periods between the decrements in loads. Similar regimes of multiple sets to exhaustion with little or no rest between the decreasing loads are often performed by bodybuilders. Choi et al. (1998) and Masuda et al. (1999) also showed that this type of regime resulted in greater increases in whole muscle area and muscle fiber area compared with a pure high-intensity (90% of 1RM) routine.

Goto et al. (2003a, 2004) investigated the effects of adding a single moderate-intensity (50% of 1RM) set performed to failure after multiple high-intensity (90% of 1RM) sets and found both larger acute increases in GH and greater increases in quadriceps muscle CSA and strength over time compared with performing only high-intensity sets. Goto et al. (2004) speculated that the greater GH response seen with the combined regime could be an important factor, but also acknowledged that the increased volume of work may have provided a stronger stimulus for muscle hypertrophy. In addition, it is possible that some local mechanisms were enhanced due to the more sustained ischemia (e.g., greater production of prostaglandins and/or phosphatidic acid in the working muscles). Because of the relatively few studies that have been performed to date on combined or hybrid regimes, further research is obviously needed to establish whether low-to-mod-

erate intensity ischemic training has an additive effect also when added to an already very effective high-intensity routine.

#### Potential disadvantages of low-load ischemic training compared with conventional heavy resistance training

Training with lighter loads implicates that compression forces on bones and joints as well as strain on tendons are reduced compared with traditional strength training. In the late 1800s, it was observed that bone architecture adapts to mechanical loading so that the trabecular patterns coincide with the trajectories of the mechanical stresses (Wolff, 1892, translated by Maquet and Furlong, 1986). Later workers have extended this concept and proposed that bone strength adapts chiefly to peak momentary loads (Frost, 2001). In support, cross-sectional studies of different types of athletes have demonstrated that adaptations in bone mineral density (BMD) are load dependent (e.g., Nevill et al., 2004). Similarly, longitudinal studies have shown that increases in BMD are greater after maximal eccentric training than maximal concentric training (Hawkins et al., 1999) and after high-load conventional strength training compared with moderate-load training (Kerr et al., 1996). Consequently, it is reasonable to assume that light-resistance occlusion training has less impact on bone metabolism than traditional high-load strength training. However, training with vascular occlusion can increase markers of bone turnover (Beekley et al., 2005), so it remains to be shown how this type of training affects bones over time and if it is a useful tool in the prevention of bone mineral loss in various situations of inactivity.

The adaptations of tendons to training vary with the mode of exercise performed (e.g., Simonsen et al., 1995; Kubo et al., 2001) and high-resistance training seems to increase stiffness of human tendons (Kubo et al., 2001; Reeves et al., 2003; Kongsgaard et al., 2007). In a recent study by Kubo et al. (2006), young males trained one leg with high-load (80% of 1RM) dynamic knee extensions and the other with low-load (20% of 1RM) knee extensions under conditions of vascular occlusion. After 12 weeks of training, both protocols resulted in significant increases in muscle strength, and the gains in muscle volume of the quadriceps femoris were similar for the two limbs. However, only the high-load protocol significantly increased stiffness in the tendon–aponeurosis complex. Furthermore, only the leg that had been trained with the high-load protocol showed increases in EMG, muscle activation and specific tension. In

support of the importance of load or strain magnitude, Arampatzis et al. (2007) reported increased Achilles tendon stiffness and CSA after 14 weeks of training with isometric contractions at 90% of MVC, whereas isometric contractions at 55% of MVC had no effect on the tendon stiffness or CSA. In summary, it seems reasonable to suggest that while the effects of blood flow-restricted training at low loads and traditional heavy-resistance training on muscle volume are similar, the effects of low-load ischemic training on tendons, and possibly also on neural adaptations, are less than with conventional strength training.

#### Perspectives

The research on resistance exercise performed during ischemic conditions has so far provided important new insights into the physiology of strength training. In addition to being a possible alternative or complement to conventional high-load resistance training in certain situations, ischemic strength training may also have a place in sports training. Because relative ischemia can be induced at rather low loads in certain exercises even without tourniquets, external pressure may not always be necessary to achieve significant training effects. Also, any unique effects of cuff occlusion *per se* during exercise have yet to be determined because the increased training effects observed in the studies published to date may simply have been due to greater effort. With reference to training combined with cuff occlusion, current evidence suggests that this mode of exercise is relatively safe, but more research is needed especially regarding the potential adverse effects on soft tissues.

**Key words:** strength training, ischemia, vascular occlusion, muscle hypertrophy, muscle atrophy.

**Note:** Shortly after this paper was accepted, a study by Drummond et al. (2008) reported no change in MGF mRNA, but a downregulation of myostatin mRNA in biopsies obtained from human vastus lateralis 3 h after low-intensity (20% of 1RM) knee extensions performed with and without blood flow restriction.

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