Where Does Blood Flow Restriction Fit in the Toolbox of Athletic Development? A Narrative Review of the Proposed Mechanisms and Potential Applications

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Abstract

Blood flow-restricted exercise is currently used as a low-intensity time-efficient approach to reap many of the benefits of typical high-intensity training. Evidence continues to lend support to the notion that even highly trained individuals, such as athletes, still benefit from this mode of training. Both resistance and endurance exercise may be combined with blood flow restriction to provide a spectrum of adaptations in skeletal muscle, spanning from myofibrillar to mitochondrial adjustments. Such diverse adaptations would benefit both muscular strength and endurance qualities concurrently, which are demanded in athletic performance, most notably in team sports. Moreover, recent work indicates that when traditional high-load resistance training is supplemented with low-load, blood flow-restricted exercise, either in the same session or as a separate training block in a periodised programme, a synergistic and complementary effect on training adaptations may occur. Transient reductions in mechanical loading of tissues afforded by low-load, blood flow-restricted exercise may also serve a purpose during de-loading, tapering or rehabilitation of musculoskeletal injury. This narrative review aims to expand on the current scientific and practical understanding of how blood flow restriction methods may be applied by coaches and practitioners to enhance current athletic development models.

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Key Points

Both resistance and endurance exercise may be combined with blood flow restriction to provide a broad range of adaptations in skeletal muscle, benefitting both muscular strength and endurance qualities concurrently, which are necessary for athletic performance in most sports.

High-frequency blocks of blood flow restriction training may also selectively target satellite cells and promote myonuclear accretion, thereby priming skeletal muscle to attain greater hypertrophy in subsequent blocks of traditional high-load training.

Practitioners and coaches may also use blood flow restriction exercise in their periodisation models to supplement or de-load from traditional high-intensity training, or to accelerate recovery from musculoskeletal injury.

Further research is warranted to optimise these approaches in athletic cohorts and to evaluate their practical merit.

1 Introduction

Performing exercise under partial blood flow restriction (BFR) has garnered much interest in recent years, owing to the potential to produce marked skeletal muscle hypertrophy and increases in strength with low training loads [1]. In particular, the magnitude of hypertrophic adaptations to resistance training (RT) is like that observed with traditional high-load RT (HL-RT), even when very low loads (< 30% of 1 repetition maximum [1RM]) are performed in conjunction with BFR [2]. Consequently, this method of exercise is recognised to have important implications for populations who cannot tolerate high levels of mechanical load, or would benefit from targeted periods of reduced mechanical stress. Such populations include the frail elderly [3] and those returning from musculoskeletal injury [4], but this also extends to athletic populations [5].

Evidence continues to emerge that athletes can use BFR to maximise various aspects of physical development, including both muscular strength and endurance capabilities [6–11]. Traditionally, it has been thought that these divergent phenotypes in skeletal muscle are dichotomous, and require different training protocols [12]. However, recent data suggest that both endurance and RT under BFR can

elicit hypertrophic and oxidative capacity adaptations simultaneously [6, 7, 9]. This dual ability of BFR training makes it an attractive choice for many athletes because it can reduce the number of sessions required to maintain and develop such physical qualities. More recently, there has been a shift in the literature to understand whether the combination of low-intensity BFR in conjunction with traditional HL-RT provides a synergistic effect on training adaptations [6, 8, 13, 14]. These data provide another avenue through which coaches and their athletes may use BFR training to optimise athletic development.

Despite the literature supporting the use of BFR in athletes, evidence suggests that practitioners and coaches often limit its use to rehabilitation from musculoskeletal injury, both in athlete and non-athlete populations [15]. Presumably, this may be because of the limited scientific understanding on how healthy athletic cohorts should adopt this mode of exercise training, and how it should be prescribed in conjunction with more typical high-intensity training methods. Applications of BFR in general populations [16] and well-trained individuals and athletes [17] have been provided previously. However, some updated recommendations are warranted to reflect the significant amount of novel information now available, particularly with athletes.

In this narrative review, we evaluate the efficacy of BFR as an additional training method for athlete populations and outline several potential mechanisms of action. We also propose several novel strategies to inform practitioners on how to best use BFR exercise to supplement traditional high-load training to maximise athletic performance.

2 Phenotypic Adaptations to Training

2.1 Adaptations Towards a Strength and Power Phenotype

When BFR is combined with RT (BFR-RT), the principal adaptation is skeletal muscle hypertrophy. Studies consistently demonstrate increases in skeletal muscle size, both at the micro level (i.e. increases in myofibre area) [6, 18–20] and at the macro level (i.e. increases in muscle cross-sectional area [CSA]) [3, 6, 21–23] following BFR-RT, which are commensurate with HL-RT [2]. Importantly, this holds true even in well-trained and athletic cohorts [6, 24]. Muscular strength is also frequently reported to increase with BFR-RT [25–27]. Seemingly, strength adaptations to low-load (LL) RT can be enhanced with the addition of BFR [28]; however, these adaptations are often inferior to traditional HL-RT [2]. An in-depth discussion of the potential reasons for these divergent strength gains between LL-BFR and HL-RT is provided elsewhere [29, 30]. One possible reason for this discrepancy is sub-optimal neural adaptation

following LL-BFR, which alongside hypertrophy, also mediates increases in strength [30]. It may be that the highest threshold motor units and muscle fibres are only briefly recruited during LL-BFR, particularly when sets are completed with a fixed repetition scheme (i.e. not to failure) [29]. This may also be compounded by the inhibitory influence of group III/IV afferent input to the central nervous system (CNS). Group III afferents, specifically, are sensitive to metabolic perturbations [31], and thus the activation of these afferents is related to the degree of ischaemia and the amount of active muscle mass during exercise [29]. Such afferent input may limit the firing rates of the highest threshold motor units. If the discharge rates of these units are limited consistently (by exclusively performing LL-BFR), this may limit maximal adaptation within the CNS. There is a paucity of literature comparing neural adaptations following LL-BFR and HL-RT [30]. However, some evidence in untrained individuals suggests that voluntary activation tends to increase with HL-RT, with negligible changes following LL-BFR [32, 33]. Hypothetically, such differences in neural adaptations and strength outcomes between protocols may be exacerbated in athletic cohorts, owing to elevated baseline levels of neuromuscular function. Other plausible explanations for the lower increases in strength with LL-BFR compared with HL-RT may be differences in structural and architectural adaptations, such as changes in tendon properties, muscle length and fascicle pennation angle in pennated muscles. There is, however, conflicting results on the impact on tendon properties [33–35] and information on possible differences in muscle length and architecture is lacking. Despite the inferior effect on muscle strength, it is important to note that muscular strength does not diminish, and still improves marginally following LL-BFR — even when adopted for prolonged periods in well-trained individuals [24]. Indeed, when HL-RT and LL-BFR are combined together in the same training programme (as we propose later in this review), slow-velocity strength adaptations may be superior compared with HL-RT alone [14, 36].

The influence of BFR on power-based qualities of the neuromuscular system is less certain. In theory, because power is the product of force and velocity, power may be enhanced somewhat with BFR through the development of strength. However, the velocity of muscle contraction is typically much slower with BFR-RT than traditional sprint or power training [37], which is likely due to: (i) the high degree of fatigue that is often generated by high repetition numbers and metabolite accumulation [38] and (ii) the intentional performance of repetitions at slower velocities and without maximal effort, seemingly to prolong time under tension. Furthermore, in contrast to HL-RT, adaptations to LL-BFR may favour slower-contracting, type I muscle fibres (discussed further below) [6, 39]. These notions are supported by results from a handful of studies that used jump or sprint performance as methods of assessing the impact of LL-BFR on lower body power. No improvements in vertical jump height [8, 40], horizontal jump distance [41] or sprint speed [8] were observed in these studies. Therefore, BFR-RT performed in its typical format (with slow-velocity contractions) may not influence the capacity for high-velocity movement, which may in turn explain the lack of changes in muscular power reported in the literature. Nevertheless, some evidence suggests that parameters associated with muscular power (such as the rate of force development [RFD]) are improved, yet exhibit a delayed response following LL-BFR. Nielsen et al. [42] observed a 15–20% increase in the RFD that was only apparent 12 days after the final LL-BFR training session. It is possible that previous studies that demonstrated negligible changes in muscular power may have evaluated these qualities too soon following training cessation and did not capture any delayed responses in these high-velocity movement qualities.

Moreover, muscular power may also be improved when BFR is applied in a less-conventional format. For example, the combination of BFR during sprint training enhanced RFD during an isometric leg press task and improved sprint time in a 100-m effort [43]. In addition, muscle thickness, used as a proxy indicator of muscle hypertrophy, simultaneously increased in the BFR condition [43]. Similarly, maximal power during a countermovement jump, and sprint time were enhanced in elite rugby players when BFR was applied intermittently (during working periods only) with HL-RT (70% 1RM) [27]. When BFR was applied during high-velocity knee extension training (300°/s), peak torque produced during a high-velocity maximal voluntary contraction increased beyond the same training without BFR [44]. Acutely, BFR may also be used with low-volume, high-load resistance exercise (HL-RE) to elicit a post-activation performance enhancement [45, 46]. Improvements in bench press bar velocity and power have been observed following a high-load BFR protocol that consisted of three repetitions at 70% 1RM [46]. Together, these data suggest that conventional LL-BFR has a negligible influence on muscular power; however, additional benefits (both acute and chronic) may be derived from combining BFR with high-intensity or high-velocity anaerobic training.

2.2 Adaptations Towards an Endurance Phenotype

Typically, the specificity of the morphological and functional adaptations obtained by skeletal muscle depend on the implemented training modality [47]. Resistance training upregulates anabolic processes that ultimately translate to the chronic outcomes of muscle hypertrophy and strength gain [48]. Conversely, endurance training upregulates genes responsible for mitochondrial biogenesis and angiogenesis, which serves to improve metabolic functioning and enhance

oxidative capacity and aerobic performance [49]. Interestingly, when BFR is combined with low-intensity endurance exercise, it appears that both hypertrophic and oxidative muscular adaptations can be simultaneously achieved. Conceição et al. [7] demonstrated that the combination of BFR with low-intensity cycling training can promote concurrent improvements in muscle CSA, strength and $\dot{V}O_{2max}$. Of interest, the gains in CSA following BFR cycling were comparable to that observed with a traditional HL-RT condition, which involved leg press exercise. Furthermore, $\dot{V}O_{2max}$ improved in the BFR cycling condition, despite the reduction in training intensity (40% $\dot{V}O_{2max}$) compared with the traditional endurance group (70% $\dot{V}O_{2max}$). Another study involving well-trained cyclists reported that applying BFR in the recovery periods during sprint interval training significantly improved $\dot{V}O_{2max}$ (~ 5%) above the same training without BFR [50]. However, this did not translate to improved cycling time-trial performance.

In contrast to the effect of traditional non-BFR training, both endurance and RT with BFR appear to influence local muscular endurance profoundly [8, 26, 51, 52]. Often, this is demonstrated by increased work, for example, volume or kilojoues completed before muscular failure occurs [8, 26], which is likely driven by the various mitochondrial and angiogenic mechanisms described below. The ability to offset fatigue-related impairments in performance is a valuable quality that transfers to a diverse range of sports. Crucially, improvements in local muscular endurance can occur simultaneously with muscle hypertrophy and muscular strength using BFR, which have traditionally been thought to be opposing adaptations in skeletal muscle [12].

3 Postulated Mechanisms of Action

3.1 Anabolic Signalling and Myofibrillar Protein Synthesis

The primary cellular mechanism through which LL-BFR purportedly enhances protein synthesis rates involves the mammalian target of rapamycin (mTOR) pathway [53]. The mTOR complex 1 acts as a key intracellular signalling protein that activates several downstream anabolic effectors [54]. The importance of this protein in the hypertrophic response to LL-BFR is demonstrated by the impaired muscle protein synthesis responses to exercise when rapamycin, a pharmaceutical inhibitor of mTOR, is administered [55]. Moreover, we have demonstrated that the upstream activation of the mTOR pathway is similar between LL-BFR and HL-RT [24], despite the differing contributions of mechanical and metabolic stimuli. In this instance, phosphorylation of several key protein kinases within both the mTOR and extracellular signal-regulated kinase pathways were similar

following LL-BFR and HL-RT, and this translated into comparable hypertrophy following 9 weeks of training.

3.2 Ribosomal Biogenesis

Alongside increases in muscle protein synthesis, another acute molecular response that occurs following a bout of resistance exercise (RE) is ribosomal biogenesis [56]. In the hours following exercise, increased transcription of ribosomal DNA occurs, and this is responsible for the accumulation of ribosomal RNA (rRNA), which is believed to precede hypertrophy [57]. Increases in ribosomal content would permit greater translational capacity, meaning the manufacture of contractile proteins is augmented. This is supported by evidence that RNA synthesis correlates strongly with muscle protein synthesis [56, 58, 59], with > 85% of total RNA being rRNA [60].

Recently, studies have investigated the influence of LL-BFR on rRNA responses. For example, we showed that LL-BFR acutely increases the expression of early rRNA transcriptional factors, such as c-Myc, transcription initiation factor IA and TATA box-binding protein-associated factor 1A, to a similar degree as HL-RT [24]. Further, Sieljacks et al. [59] demonstrated that LL-BFR increased cumulative RNA synthesis and total RNA content, again similar to HL-RT, after 6 weeks of training. The comparable responses between LL-BFR and HL-RT in stimulating ribosomal biogenesis may be driven through their similar activation of mTOR [24], which may be partly responsible for increases in rRNA [61]. This notion comes from evidence that inhibiting mTOR by rapamycin also blunts the increase in total RNA content and ultimately hypertrophy [62]. Together, these data suggest that both LL-BFR and HL-RT stimulate ribosomal biogenesis and that this process constitutes one underlying factor determining the muscle hypertrophic response to these two exercise protocols.

3.3 Satellite Cell and Myonuclear Responses

Another mechanism through which BFR has been proposed to drive skeletal muscle hypertrophy is through activation of myogenic stem cells, known as satellite cells (SCs) [19]. Under certain conditions, SCs are activated to facilitate muscle repair and regeneration, as well as to provide new myonuclei during hypertrophy. Interestingly, SC proliferation is especially pronounced following high-frequency LL-BFR [18, 19], despite reduced loading conditions and often in the absence of typical biomarkers of muscle damage (e.g. creatine kinase) [63]. This suggests that BFR exercise may induce sufficient (and potentially excessive) myocellular stress, without overt structural damage. Several high-frequency BFR training studies (five or more sessions per week) support this notion; showing large increases in SC

proliferation, alongside prolonged impairments in muscle function [18, 42, 64] and other markers of cellular stress, such as heat shock protein accumulation [63]. Interestingly, heat shock protein accumulation tended to occur at the myofibre membrane with LL-BFR, as opposed to a more granular myofibrillar staining pattern, which is more common following muscle damaging exercise [65].

Activating the SC pool adds myonuclei to existing muscle fibres, which supports the maintenance of a fixed cytoplasmic volume-to-nucleus ratio (also termed the *myonuclear domain*). A key rationale for such training-induced myonuclear addition is to provide more rDNA template to facilitate ribosome biogenesis (discussed above), which may be required to support the increased cytoplasmic volume of the growing myofibre [61]. Therefore, the addition of myonuclei would support rRNA transcription and diffusion throughout the myofibre, ultimately amplifying the hypertrophic response to RT through increased translational machinery. Importantly, although SC activation seems to be a transient process that may return to baseline levels quickly following 10–14 days of LL-BFR training [19], the newly acquired myonuclei seem to be maintained. Therefore, LL-BFR may serve as a strategy to target myonuclear accretion (and thus increased transcriptional capacity) through SC activation, when performed in 1- to 2-week blocks interspersed with traditional HL-RT [6]. In support of this notion, Nielsen et al. [19] and Bjørnsen et al. [6, 18, 64] have reported increases in myogenic SC numbers that range from ~100 to 200%, and increases in myonuclei content of ~20 to 30%, following ~20 days of high-frequency BFR training (five or more sessions per week). Such a robust increase in myonuclei content vastly exceeds the typical gains of ~9% during a longer duration (i.e. 16 weeks), traditional RT regime [66]. It is, however, important to acknowledge that the high-frequency protocols used in these LL-BFR studies generate substantial cellular stress [67] and prolonged decrements in muscle function [18, 42, 64], and therefore must be gradually introduced and used with caution. For example, in the study by Bjørnsen et al. [18], muscular strength was impaired (−4%) 4 days following the high-frequency BFR block and only peaked (+6%) after 20 days of detraining.

The mechanism responsible for the potent activation of the SC pool by BFR exercise is not clear. However, one possible mechanism involves nitric oxide-induced synthesis of hepatocyte growth factor [53]. Nitric oxide synthase is linked to both mechanical stretch and shear stress [68], and increases acutely in muscle following LL-BFR [69]. Downstream of nitric oxide synthase, matrix metalloproteinases may mediate hepatocyte growth factor release from the extracellular matrix [68]. Once released, hepatocyte growth factor binds to its c-Met receptor, and consequently activates quiescent SCs in a dose-dependent manner [70]. Activation of the SC pool may also result from the downregulation of

myostatin [71]. It has been reported that LL-BFR reduces myostatin gene expression [72], potentially by downregulating the messenger RNA (mRNA) expression of myostatin receptor activin IIb [73]. Myostatin is known to inhibit SC proliferation; accordingly, its downregulation may contribute to the robust activation of SCs described above [72].

3.4 Mitochondrial and Angiogenic Responses

As discussed earlier, both resistance and endurance exercise combined with BFR elicit improvements in oxidative capacity [7, 50, 74] and local muscular endurance [8, 26, 51, 52]. Typically, such improvements are achieved in part by activating peroxisome proliferator-activated receptor gamma coactivator 1-α (PGC-1α), which is known as a master regulator of mitochondrial biogenesis [75]. Genes related to angiogenesis, like vascular endothelial growth factor, are also upregulated to support the expansion of new vasculature (enhanced capillarisation) and the development of existing blood vessels [76]. Whereas traditional endurance training upregulates both of these adaptive pathways, Conceição et al. [77] found that 15 min of BFR cycling did not increase mRNA expression of any of the isoforms of PGC-1α. However, in a subsequent study, the same authors found that 30 min of BFR cycling increased mRNA expression of cytochrome c subunit 4 isoform 1 [7], which is another marker indicative of mitochondrial biogenesis. Furthermore, a study by Christiansen et al. [78] observed increases in PGC-1α mRNA abundance following exercise when BFR was combined with interval running. The higher intensity of exercise used in the study by Christiansen et al. (105% of lactate threshold) may explain the greater effect on PGC-1α, which has been shown to respond in an intensity-dependent manner [79]. Notably, mitochondrial biogenesis is initiated by the translocation of PGC-1α from the cytosolic to the mitochondrial and nuclear compartment [49]. This activation of PGC-1α has been less studied. Additionally, more frequent cycling of hypoxia reperfusion is thought to enhance PGC-1α expression [80] and may also explain the discrepancies between studies. With regard to RT, it was recently observed that following both LL-BFR and traditional HL-RT, mitochondrial protein synthesis is elevated cumulatively, while mitochondrial respiratory function is also enhanced in untrained individuals [81]. Despite the similar mitochondrial adaptations between conditions, performance in a muscular endurance task was enhanced only in the group that trained with LL-BFR [81]. Differences in vascular adaptations induced by angiogenesis may have accounted for the disparity in endurance performance; however, capillary density was not assessed in this study. Interestingly, in strength-trained men and women, we have recently observed that levels of mitochondrial enzymes (e.g. citrate synthase, COX4) increase by 15–50% after 9 weeks

of LL-BFR, whereas no change (or even a reduction) was observed in the same mitochondrial enzymes following HL-RT [82].

Previous studies have identified a robust increase in genes related to angiogenesis following acute RE with BFR [7, 69, 83, 84]. Hypoxic-inducible factor-1 is one such gene that is expressed following exposure to low-oxygen environments. Downstream targets of hypoxic-inducible factor-1 include vascular endothelial growth factor, which serves to enhance tissue function during low oxygen availability [76]. Vascular endothelial growth factor gene expression is routinely upregulated following both resistance and endurance exercise when combined with BFR [69, 76, 85], which can translate into enhanced capillarisation, in as little as 2 weeks [86]. In support of this notion, capillaries around type I fibres increased with LL-BFR training in a group of highly trained individuals, and this increase tended to be greater compared with those athletes who performed HL-RT only [6]. Another study (albeit in untrained individuals) observed a 15–16% increase in the capillary-to-muscle area ratio and thickening of the perivascular basal membrane following only 3 weeks of LL-BFR [87]. In the study described above by Conceição et al. [7], improvements in aerobic capacity were strongly associated with increases in angiogenic factors, as opposed to typical markers of mitochondrial biogenesis. Together, these findings suggest both endurance and RE combined with BFR can induce mitochondrial and angiogenic adaptations in skeletal muscle. In turn, these adaptations may be responsible for the improved aerobic capacity and muscular endurance performance that is often reported following training with BFR.

3.5 Fibre-Type Specificity

A contentious issue in the current literature is the notion that BFR exercise may be used to target either type I or type II fibres preferentially. Few studies have employed the invasive biopsy techniques necessary to distinguish between fibre types, and to evaluate recruitment patterns, acute metabolism and chronic structural adaptations. Early research has clearly demonstrated that during LL-BFR, the full spectrum of fibre types is recruited to maintain force output—providing that sufficient volume is performed and the degree of fatigue is close to maximal [38, 88, 89]. Evidence of this is provided by the significant metabolite depletion (e.g. phosphocreatine, glycogen) in the larger type II fibres following BFR-RT, despite the use of low loads [39, 90]. However, more recent evidence suggests type I fibres may be subjected to greater stress with LL-BFR [6, 18, 39, 67, 91]. Specifically, this evidence stems from reports of greater heat shock protein responses and glycogen depletion in type I fibres following

LL-BFR—even when sets are carried out until muscular failure [39, 67]. Wernbom and Aagaard [29] have suggested that motor unit recruitment patterns during LL-BFR may deviate from the Henneman size principle. Specifically, LL-BFR may preferentially utilise type I muscle fibres, which have a greater ability to tolerate low-oxygen conditions. The superior recovery capacity of type I fibres may also favour their continued recruitment across multiple sets of LL-BFR following the fatigue (and potential dropout of type II fibres) [29]. The recruitment pattern outlined above may explain how type I fibres are exposed to a greater stimulus following multiple sets of BFR exercise [29].

Factors such as training status and exercise selection may also play a role in determining which fibre types are exposed to the most stress, and subsequently adapt the most. In untrained populations, the relative increase in muscle fibre area following training appears to be equal between type I and type II fibres [19]. However, in a cohort of elite powerlifters, well accustomed to strength training, muscle fibre area appeared to increase solely in type I fibres, and myonuclei addition and capillarisation were also restricted to type I fibres [6]. Such findings may suggest that the type II fibres of these trained individuals are already well developed with their normal HL training, and there is a minimal additional effect from the LL-BFR stimulus. The use of BFR with bilateral compound exercises (such as the front squat, which was used in the study with powerlifters) may also stimulate group III/IV afferents within the muscle to a greater extent compared with single-joint unilateral exercises [29]. As discussed above, afferent input to the CNS may lead to submaximal recruitment and firing rates in high-threshold motor neurons that innervate type II fibres [29]. Taken together, this may explain why preferential adaptation was observed in type I fibres when a cohort of highly trained individuals performed bilateral compound exercises with BFR [6]. However, in untrained populations, and/or when performing unilateral single-joint exercises with BFR, there may be a more balanced stress application, and subsequent adaptation between type I and type II fibres. Nevertheless, the partitioning of stress across fibre types with BFR appears to be in contrast to traditional HL-RT, following which preferential type II fibre adaptation usually occurs in both untrained and trained individuals [48]. Together, these data suggest that LL-BFR can promote adaptations across both fibre types; however, there may be greater stress and subsequent adaptation in type I fibres, when compared with conventional HL-RT. Thus, LL-BFR in combination with conventional strength training may be of importance to optimise adaptation of both fibre types, and enhance functional outcomes such as strength and muscular endurance in highly strength-trained individuals.

4 Athletic Applications

From the documented physiological effects reviewed in the first part, it is clear that even for athletes, who can tolerate high loads and intensities, BFR with low loads or intensities may also prove to be a valuable tool. Using this novel mode of exercise in conjunction with traditional training methods may provide a means to optimise physical development. Combining mechanical and metabolic stimuli could potentially elicit superior training adaptations (including both myofibrillar and oxidative capacity adaptations), compared with conventional training practices alone. However, if prescribed inappropriately, BFR exercise could significantly impair neuromuscular performance by generating considerable fatigue [18, 42], myocellular stress [63, 67] and in some cases, severe muscle damage [92, 93]. Thus, we feel it is important to provide practitioners and coaches with evidence-based recommendations for how to best use this mode of exercise with their athletes (Table 1). Potential avenues whereby BFR can be applied to athletic cohorts are discussed forthwith.

4.1 Supplemental BFR Exercise

Low-load BFR training is well tolerated and efficacious in a diverse range of athletes, with improvements observed in several pertinent outcomes, including muscle CSA [6, 25, 41], strength [6, 14, 27], local muscular endurance [8, 26] and sport-specific performance tests [26, 27, 41]. Despite this, LL-BFR should not be seen as a replacement or surrogate for conventional training methods with high loads/intensities, which remain the gold standard training strategies for athletic development. Emerging evidence suggests that high loading conditions may not be required for optimal bone [94] and tendon responses [34, 35]; nevertheless, it appears that high loads do promote superior strength [2] and power development [40], potentially mediated through enhanced neural and structural adaptations. Indeed, muscular adaptations to LL-BFR training are enhanced when integrated with traditional HL-RT [95]. Consequently, there has been a shift towards the use of LL-BFR as an additional supplementary stimulus to traditional training practices.

4.1.1 Same-Session Supplementary BFR

Performing BFR exercise after completing regular high-load exercise within a single session enhances bench press [14] and back squat [14, 36] 1RM in well-trained American football players. Despite these strength improvements, hypertrophy (as inferred by girth measurements) only appeared to increase in the chest, with no differences in arm or thigh girth compared with a control group who completed LL training without BFR [14]. The use of such anthropometric measurements as proxy indicators of muscular hypertrophy in these studies is a limitation.

To address this, Scott et al. [8] used ultrasound to measure muscle thickness in a 5-week training study involving Australian rules football athletes. Despite positive changes in strength and muscular endurance qualities over the training period, supplemental BFR training (following the completion of HL-RT) did not appear to enhance these attributes above the same training without BFR. Moreover, there were no significant changes in either condition for muscle thickness, and performance during sprinting and jumping tasks. It is unclear why the training did not result in muscular hypertrophy, given the findings from other studies that BFR promotes hypertrophic adaptations even in well-trained participants [25, 26, 41]. The authors proposed a possible interference effect caused by concurrent endurance training, as field-based conditioning sessions were completed immediately following the RT sessions with BFR [8]. Therefore, if optimal hypertrophy is desired it may be critical to consider the timing of concurrent training in relation to BFR training, which also is the case for traditional HL-RT. The 5-week training period might also have been too short to induce more robust adaptations in these well-trained athletes. Together, these data suggest supplemental BFR exercise performed in the same session as HL-RE may augment strength beyond HL-RE alone. Hypertrophic responses to same-session supplemental BFR exercise are, however, less clear, and warrant further investigation using gold-standard imaging measurement techniques (e.g. magnetic resonance imaging) and longer training blocks (> 6 weeks).

4.1.2 Separate Session/Block BFR

Conversely, supplementary BFR training may be completed in separate sessions or blocks from traditional training. A common approach in the literature is a block of high-frequency (five or more sessions/week) BFR training interspersed with traditional high-load training. As with same-session supplementary BFR exercise, separate sessions or blocks where LL-BFR exercise is exclusively performed could theoretically be used amongst HL-RT to provide a well-rounded stimulus for skeletal muscle (comprising metabolic and mechanical components). Moreover, the maintenance of an adaptive stimulus, despite shorter session durations, and lower mechanical load and volume may provide benefit through the management of the training load.

Supplemental BFR in separate sessions or blocks has not been investigated in athletic cohorts. However, studies using recreationally active individuals may offer some guidance in this area. Yasuda et al. [95] reported that combining LL-BFR and HL-RT in separate sessions (2×LL-BFR,

Table 1 Evidence-based recommendations for the use of BFR training for performance enhancement and injury management in a range of different sports and athletic populations

Desired outcome	BFR applications	Type of sport/athlete
Improve muscular development Increase muscle hypertrophy [6, 25, 26, 41] Increase muscular strength [41, 42, 103] Increase satellite cell proliferation [18, 19]	Supplemental BFR training (resistance training) Sport-specific BFR training High-frequency BFR block during off-season or pre-season	Team sports (e.g. soccer, netball, rugby) Racquet sports (e.g. tennis, squash) Centimetre, gram, second sports (e.g. power-lifting, track and field, swimming) Combat sports (e.g. mixed martial arts, boxing)[a]
Improve local muscular endurance Increase buffering capacity [8, 26, 97, 98] Increase capillary formation [87] Increase artery diameter [52, 141] Increase mitochondrial content [81, 82]	Supplemental BFR training (resistance training) Supplemental BFR training (endurance training) Sport-specific BFR training High-frequency BFR block during off-season or pre-season	Team sports (e.g. soccer, netball, rugby) Racquet sports (e.g. tennis, squash) Endurance sports (e.g. triathlon, long course cycling) Centimetre, gram, second sports (e.g. power-lifting, track and field, swimming) Combat sports (e.g. mixed martial arts, boxing)
Improve aerobic capacity Increase maximal oxygen uptake [7, 142] Increase running economy [97]	Supplemental BFR training (endurance training) Sprint interval training with BFR during recovery periods Sport-specific BFR training	Team sports (e.g. soccer, netball, rugby) Racquet sports (e.g. tennis, squash) Endurance sports (e.g. triathlon, long course cycling) Combat sports (e.g. mixed martial arts, boxing)
Support musculoskeletal rehabilitation Limit muscle atrophy [114, 124, 126, 129] Limit strength loss [115, 126, 129] Limit reduction in oxidative capacity [74, 125] Pain reduction [131, 132] Potential fracture healing [116, 118–120]	Cyclical BFR during passive rest or NMES BFR applied during walking or low-intensity cycling BFR combined with bodyweight exercises and light resistance Supplemental BFR training (resistance training)	Team sports (e.g. soccer, netball, rugby) Racquet sports (e.g. tennis, squash) Endurance sports (e.g. triathlon, long course cycling) Centimetre, gram, second sports (e.g. power-lifting, track and field, swimming) Combat sports (e.g. mixed martial arts, boxing)
Improve performance in sport-specific tasks Improved sprint performance [27, 41, 140] Improved change of direction [140]	Supplemental BFR training (resistance training) High frequency BFR blocks Sport-specific BFR training[b]	Team sports (e.g. soccer, netball, rugby) Racquet sports (e.g. tennis, squash)
Training load management Improvements in hypertrophy, strength, power, and endurance with reduced volume [111] Concurrent muscular and mitochondrial adaptations from single session [7, 82]	Supplemental BFR training (resistance training) Supplemental BFR training (endurance training) High-frequency BFR blocks	Endurance sports (e.g. triathlon, long course cycling) Centimetre, gram, second sports (e.g. power-lifting, track and field, swimming)
Post-activation performance enhancement in strength and power tasks [45, 46]	BFR during low-volume high-intensity priming exercise	Centimetre, gram, second sports (e.g. power-lifting, track and field, swimming)

Several BFR applications are presented for each sport/athlete. Desired outcomes are supported with evidence using relevant athletic populations, or well-trained individuals, where possible

BFR blood flow restriction, *NMES* neuromuscular electrical stimulation

[a]Hypertrophy may be undesirable in some combat sport athletes because of the use of weight classes. It is recommended that the use of BFR is carefully considered in these sports

[b]The metabolic demand is increased with BFR during sport-specific training, which may impair the movement quality and coaches should therefore carefully consider the possible benefits on physiological adaptations vs possible negative effects on the technical execution of drills

1×HL-RT per week) provided superior strength gains to LL-BFR alone. However, muscle CSA and strength following the combined training were comparable to HL-RT alone. One limitation of this study was that only HL-RT progressed in load across the 6 weeks, whereas the load remained the same for LL-BFR. Thus, LL-BFR sessions may not have induced an optimal stimulus. More recently, one study explored alternating weekly blocks of LL-BFR and HL-RT for a 6-week period [13]. Similar to the findings of Yasuda et al., there was no additional benefit for muscle size or strength adaptations when LL-BFR blocks were included in the training, compared with HL-RT alone. Of interest, no elevations in SC content or increases in myonuclei number were observed with the group that alternated between LL-BFR and HL-RT, in contrast to other LL-BFR studies (which are discussed below). Together, these data

suggest that including LL-BFR training in separate sessions or blocks alongside HL-RT does not compromise muscle strength or size adaptations (and may preferentially target type I fibres); however, the inclusion of LL-BFR training may not provide overall greater strength or size adaptations to HL-RT alone. Further study of integrated programs combining LL-BFR and HL-RT, particularly involving athletes, is warranted.

4.1.3 Sport-Specific BFR Training

A novel use of BFR that has emerged in recent years is its application during sport-specific training. A handful of studies have reported that BFR during soccer-specific or futsal-specific training, such as small-sided games and drills, may improve various physical attributes above and beyond the same training performed without BFR. The application of BFR during futsal small-sided games was observed to increase levels of anabolic hormones and isometric knee extension strength [96], and anaerobic power and running economy [97] more than the group that trained without BFR. The authors postulated that the improvements in anaerobic and aerobic performance were likely because of local muscular adaptations, as improvements in $\dot{V}O_{2max}$ were not different between groups [97]. Additionally, there tended to be larger improvements in a futsal-specific performance test in the BFR group, with large effect sizes observed. However, this was not statistically significant. The lack of statistical significance in some physical variables may be because of the short training intervention of 3 weeks (ten sessions).

More recently, Hosseini Kakhak et al. [98] performed a longer training intervention lasting 6 weeks (18 sessions) in soccer athletes. Significantly greater improvements were noted in the tests of aerobic power, sport-specific endurance, change of direction and muscular endurance following training with BFR. Performance in strength and power tests also improved; however, these were not significantly different between groups. Taken together, these studies suggest that sport-specific training combined with BFR exacerbates the metabolic demands of the drills, thus facilitating improvements in the buffering capacity of skeletal muscle and fatigue resistance. These findings are particularly relevant for coaches and practitioners who are required to concurrently develop numerous physical attributes in team sport athletes, while also improving their technical and tactical skills.

4.2 High-Frequency Blocks

When individuals are unaccustomed to LL-BFR, this mode of exercise can induce significant muscle damage [92, 93], and prolonged decrements in force that are similar to unaccustomed eccentric exercise [99]. Despite this, once individuals become accustomed to LL-BFR (through protective adaptations, such as the repeated bout effect [100]), most data tend to suggest that the risk of muscle damage is similar to conventional HL-RT [39, 63, 99]. Recovery of exercise-induced impairments in neuromuscular function also appears to be very rapid [101, 102]. This has led some authors to suggest that higher training frequencies may be tolerated, which in turn may accelerate and augment adaptations within skeletal muscle. Some studies have successfully implemented training frequencies as high as twice daily [20, 41, 103, 104]. Following training blocks of 1–2 weeks (during which 12–24 sessions were completed), hypertrophy and strength improvements are similar in magnitude to those observed following much longer (i.e. 8–12 weeks) traditional HL-RT programmes [18–21, 41, 42, 104]. Such an approach was applied to elite powerlifters in a recent study, where two 1-week blocks of high-frequency LL-BFR training (five sessions per block) were interspersed amongst more typical high-load (~85% 1RM) training [6]. Following the 7-week training period, the LL-BFR and HL-RT group demonstrated greater hypertrophy and increase in isokinetic strength than HL-RT only, which were both correlated with increases in the type I fibre area. These data promote the use of high-frequency BFR blocks as a strategy to target type I muscle fibres in strength-trained individuals, drive SC proliferation and enhance the myonuclear number.

As higher training frequencies with LL-BFR are seemingly well tolerated [6, 41], this approach may represent a potential strategy to amplify and accelerate muscular development in periods where there is an emphasis on adaptation, such as the pre-season. It should, however, be highlighted that blocks of high-frequency BFR generate substantial myocellular stress (even if muscle damage is not observed), and especially when athletes are not familiar with LL-BFR [6]. Often this can lead to a transient over-reaching state in which myofibre size, strength and RFD are impaired initially, before supercompensation occurs [18, 42, 64]. Such protocols should therefore be carefully introduced and gradually progressed over time, to ensure that protective adaptations (i.e. repeated bout effect) can take place to minimise the risk of inducing excessive muscle stress and/or damage. Following familiarisation, frequencies of 5–7 sessions per week may be suitable, gradually building to 3–5 sets of exercise. It is recommended that sets are not initially performed until muscular failure; however, this can be introduced once the individual becomes acclimated to the BFR stimulus. For example, initially the final set of an exercise could be completed until muscular failure, before eventually progressing to completing all sets of the exercise until failure. Importantly, it is recommended that such protocols are tested early in the pre-season and avoided close to the competitive season. Finally, it must be acknowledged that it is not always feasible to fit such a high frequency of BFR sessions in an

athletic programme; particularly for team sports, which have multiple sporting and physiological targets during a training phase. However, as outlined earlier in this review, a broad range of distinct adaptations (strength, hypertrophy, muscular endurance, aerobic power) can be concurrently obtained with BFR training. Nevertheless, we advocate for a high frequency early in pre-season, when technical and tactical training volume is lower.

4.3 Managing Training Stress, De-Loading and Tapering

A key concern in elite sport is appropriately periodising training, which requires systematic planning to balance the goals of adaptation, recovery and performance [105]. An important aspect of periodisation involves phases of reduced loading and/or volume to allow for the recovery of particular tissues in the body, and to prepare for competition and/or the increased demand of the next training phase [106]. Another potential avenue in which BFR may be applied to athletes is during periods of tapering or de-loading. As discussed above, the lowered intensities and exercise volume would temporarily minimise the strain on joints, tendons, ligaments and the CNS. The recovery of muscle tissue during these periods is also a priority, which brings into question whether this would be a true 'taper' phase if BFR was used during these periods. This has yet to be investigated, which makes it difficult to speculate on the matter. Through our practical work with athletes we have explored this approach in powerlifters, anecdotally observing positive outcomes in subjective ratings of performance and recovery from the athletes. As stated above, although LL-BFR exercise can generate substantial myocellular stress and muscle damage, these outcomes appear to be minimised once an individual becomes accustomed to the stimulus, and if muscular failure is avoided [63, 99, 107, 108]. We have observed that following acclimation to LL-BFR training, robust hypertrophy signalling and expression of ribosomal RNA transcription factors still occur without prolonged decrements in neuromuscular function or other signs of muscle damage [24]. Thus, it may be possible to continue to achieve muscular development through metabolic stimuli, while simultaneously allowing muscle and other tissues to recover from the high mechanical stresses typically imposed by traditional progressive HL-RT.

Another primary concern in elite sport is managing total training stress to maximise physical performance, while also avoiding overtraining and injury [105]. Many sports require the continuous development of many different physical attributes (e.g. strength, speed, power) in conjunction with more sport-specific skills training [105]. Such a requirement demands a high number of training sessions, which can be problematic to fit into a weekly training schedule, especially

during the competitive season. The accumulation of these training loads can also be physically demanding on an athlete's body [109]. A hallmark of LL-BFR is the reduction in volume load (especially the reduction in absolute load) that is required to stimulate muscular adaptation [110, 111]. As the capacity for skeletal muscle to recover during rest periods is compromised because of a lack of oxygen, fatigue occurs earlier and with lower repetition numbers [38]. Consequently, the exercising muscles can receive a robust stimulus for adaptation, despite a potential reduction in exercise volume. Such a reduction in exercise volume serves as an efficient strategy because it minimises both total training stress, and training duration. The unique ability of LL-BFR to elicit both hypertrophic and oxidative capacity adaptations from the same stimulus means that training frequency may also be reduced [7, 52, 82]. Furthermore, the limited rest periods associated with this style of training also make it more time efficient than HL-RT.

4.4 Accelerating Return to Play Following Musculoskeletal Injury

Musculoskeletal injuries are an unavoidable consequence in elite sport, given the high training loads, physical contact and high-impact forces imposed on the body [109]. Following musculoskeletal injuries, there is often a period of immobilisation or reduced loading necessary to allow the injured tissue to recover. Such periods of reduced loading have a deleterious effect on muscle mass and function (e.g. strength, muscular endurance) [112]. Therefore, the goal during rehabilitation of a musculoskeletal injury is to mitigate and reverse such atrophy and detriments in muscle function, to accelerate a return to pre-injury conditions. However, traditional strength-based and field-based training are contraindicated early in the rehabilitation process, owing to the high levels of mechanical tension and impact forces imposed on injured tissues [4]. Blood flow restriction, both at rest and when combined with various modes of muscle contraction, is a promising avenue to commence the rehabilitation process earlier, and offset atrophy and loss of strength [113]. The ischaemic stimulus offered by BFR can preserve and promote adaptation in muscle, despite the reduced levels of mechanical stress that are imposed on the body. Ultimately, this would allow injured athletes to fast track their recovery to pre-injury conditions, and accelerate their return to play (Fig. 1).

A four-step model has been proposed by Loenneke et al. [113], which outlines how BFR could be used in the gradual progression from (i) bed rest or immobilisation, (ii) walking or low-intensity cycling exercise, (iii) LL-RE and finally, (iv) HL-RE. The first stage of this progressive model has been derived from evidence suggesting that BFR alone (without exercise) can reduce the amount of muscle atrophy [114]
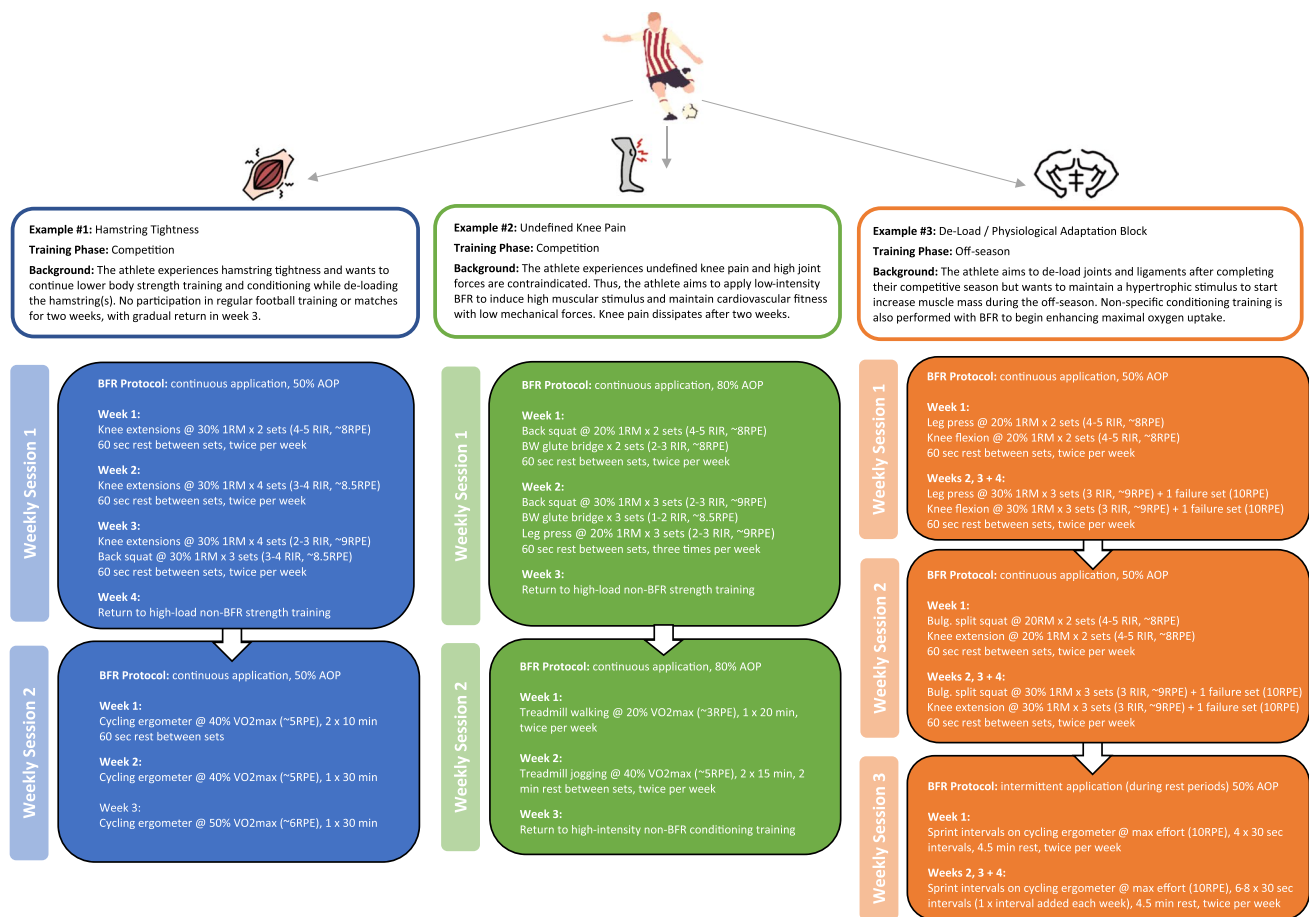
Fig. 1 Three exemplary cases of how blood flow restriction (BFR) may be introduced and progressed for a team sport athlete at various times throughout the season. The example programmes provided a focus on lower body strength and conditioning training as these are most relevant to the case study sport. Other training modes (e.g. upper body strength, sport-specific training) may continue as normal if appropriate. In situations where one repetition maximum (1RM) testing is not possible or practical, it is recommended to use a load that is estimated to be between 30 and 35 RM and to adjust effort using the repetitions in reserve (RIR) and rating of perceived exertion (RPE) values provided. If measurement of repetition velocity is possible, practitioners may also use loads that equate to initial mean concentric velocities of 1.0–1.3 m per second. *Higher cuff pressures are used in the knee pain case study as these appear to elicit a greater hypoalgesic effect [131]. *AOP* arterial occlusion pressure, *BW* bodyweight

and strength loss [115] that occurs with periods of unloading. There is also some evidence that intermittent periods of BFR may promote fracture healing [116–120]. A recent and novel addition to this early phase of rehabilitation is combining BFR with neuromuscular electrical stimulation (NMES) to induce involuntary muscle contraction. Alone, this technique appears to generate a modest degree of mechanical tension [121]; however, this is amplified under the ischaemic conditions [122, 123]. Acute studies have reported robust increases in lactate accumulation and growth hormone secretion [123], and significant neuromuscular fatigue following NMES and BFR, particularly when higher pressures are used [122]. The strength of the stimulus provided by NMES and BFR appears sufficient to inhibit muscle atrophy [124], and capillary regression [125] when repeated long term. Importantly, this stimulus can be achieved without joint movement or weight bearing, making it suitable for the initial stages of musculoskeletal rehabilitation. The use of isometric voluntary contractions may be used as a surrogate to NMES under circumstances where applying electrodes is not possible (e.g. orthopaedic casts), or access to NMES is limited.

Stage 2 of the model involves early engagement in very LL isolated activities (e.g. resistance bands) that are typical in rehabilitation programmes. The goals of such activities are to increase range of motion and develop strength, while avoiding aggravating the injured tissue. Applying BFR enhances the effectiveness of these exercises by increasing metabolic stress within the muscle [4]. In support of this notion, Ohta et al. [126] demonstrated that adding BFR to a typical anterior cruciate ligament rehabilitation programme mitigated strength losses, and improved the ratio of healthy-to-injured thigh CSA. Once weight bearing is tolerated, BFR

may be employed with walking or similar low-intensity exercise (e.g. cycling). Unlike low-intensity aerobic exercise under unrestricted conditions (i.e. without BFR), BFR during walking and cycling elicits substantial muscle hypertrophy (~5% increase in CSA) [127, 128], increases in muscular strength (~5 to 10%) [128–130] and aerobic capacity (~10%) [74] in athletic cohorts. Importantly, these modes of exercise can be employed early in the rehabilitation process of most musculoskeletal injuries, given the very low levels of mechanical stress involved.

Following this, conventional REs can be implemented with BFR using low-to-moderate loads (20–40% 1RM). A systematic review and meta-analysis demonstrated that LL-BFR is superior to LL-RT in rehabilitating musculoskeletal conditions such as anterior cruciate ligament injury and osteoarthritis and in older adults at risk of sarcopenia [4]. Data are also emerging to suggest that LL-BFR provides an acute analgesic effect, which is not observed with LL-RE or HL-RE [131, 132]. Thus, LL-BFR may also improve tolerance and adherence to rehabilitation programmes.

The final step in the model is the return to traditional HL-RT, which is likely necessary for optimal strength, power, and neural and structural adaptations [4, 133]. Although equivocal, traditional HL-RT may also be required to restore the integrity of tendons and bones [34, 134], especially if recovering from injury to these tissues [135]. However, LL-BFR may still be used as a supplement in this phase to provide a well-rounded stimulus for muscle adaptation. Specifically, following periods of detraining it appears that oxidative fibres (e.g. type I and type IIa) are negatively affected more so in trained individuals [136, 137]. We also speculate that the pronounced SC proliferations in response to high-frequency BFR training (which has been discussed earlier in this review) may serve as a potential strategy to accelerate the regeneration of muscle-based injuries, such as muscle strains. Following SC proliferation, these cells give rise to myogenic precursor cells, known as myoblasts, which ultimately form new myotubes or fuse with damaged myofibres [48]. However, no studies have examined this possibility to date. Therefore, it may be beneficial to continue to perform LL-BFR training throughout the final stages of rehabilitation, which may specifically stress oxidative fibres and drive SC proliferation, leading to preferential hypertrophic and mitochondrial adaptations [6, 39] and myofibre regeneration [48].

4.5 Safety Considerations

The safety of restricting blood flow during exercise has been rigorously investigated over the past two decades and has been reviewed extensively elsewhere [16]. Although several theoretical concerns about the safety of BFR exist, the resulting consensus is that exercise in combination with BFR poses no greater risk than regular exercise when evidence-based recommendations are followed [22, 138]. Potential complications to BFR exercise that have been proposed include vascular dysfunction, venous thromboembolism, nerve injury and elevated cardiac demand due to excessive stimulation of the muscle metaboreflex, oxidative stress and rhabdomyolysis. In healthy athlete cohorts, the risk of the above complications is thought to be extremely low [16, 139]. However, certain conditions may elevate the risk of these complications, such as peripheral vascular, cardiovascular or clotting disorders [22]. Thus, it is imperative that athletes are screened prior to commencing any BFR exercise programme using an appropriate tool [139]. As we have already alluded to earlier in this review, we recommend that BFR protocols are gradually introduced to obtain the repeated bout effect [99], and to minimise the risk of rhabdomyolysis.

5 Conclusions

Blood flow-restricted RE is currently recognised as a LL time-efficient approach to reap many of the benefits of typical HL-RT. Consequently, this method of training holds great promise for populations who cannot tolerate the high levels of mechanical stress imposed by heavy external loads. As outlined in this review, many avenues exist in which BFR may also benefit athletic development (Fig. 1). Both resistance and endurance exercise may be combined with BFR to provide a spectrum of adaptations in skeletal muscle, spanning from myofibrillar to mitochondrial adaptations. Such diverse adaptations would benefit both muscular strength and endurance qualities concurrently, which are demanded in athletic performance, especially in some team sports. High-frequency blocks of BFR training may also selectively target the SC pool and promote myonuclear accretion, thereby priming skeletal muscle to attain greater hypertrophy in subsequent blocks of traditional HL-RT. Practitioners and coaches may also use BFR exercise in their periodisation models to de-load from traditional HL-RT, or to accelerate recovery from musculoskeletal injury. Despite the promise of the applications described, it is important that practitioners and athletes introduce the BFR stimulus carefully, and gradually, to attain protective adaptations, and avoid excessive muscle damage, cellular stress and prolonged decrements in neuromuscular function. In summary, there is a plethora of theoretical avenues in which training with BFR may be applied alongside traditional practices to maximise athletic development. These approaches need to be validated in future research studies comprising athletic cohorts in order to evaluate their practical merit.

Declarations

Conflicts of interest/competing interests Charlie Davids, Llion Roberts, Thomas Bjørnsen, Jeff Coombes, Jonathan Peake and Truls Raastad have no conflicts of interest that are directly relevant to the content of this article.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material Not applicable.

Code availability Not applicable.

Authors' contributions CD and TR conceptualised the study. CD performed the literature search, interpreted the data and wrote the original draft of the manuscript. CD, LR, TB, JC, JP and TR contributed to the data interpretation and revised the manuscript. All authors read and approved the final version of the manuscript.

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