

When does nutrition add value to blood flow restriction training? A constraint-relief review of hypertrophy, strength, and fatigue resistance

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ABSTRACT

Blood flow restriction resistance training (BFR-RT) can produce hypertrophic adaptations with low external loads, but it does not consistently reproduce heavy-load strength or sport-specific outcomes. This critical narrative review asks when a nutritional adjunct might relieve a process that remains limiting after the BFR prescription and habitual diet have been optimized. PubMed/MEDLINE and citation searches were updated through 3 August 2026. A transparent relevance-based pathway retained 28 publications across direct BFR-nutrition evidence, BFR context, and indirect nutrition evidence. The proposed constraint-relief framework is explicitly presented as a conceptual, hypothesis-generating heuristic rather than an empirically validated model. In the retained 2026 meta-analysis, nutritional intervention did not provide statistically clear average evidence of additional maximal strength (7 studies; standardized mean difference [SMD] = -0.09, 95% confidence interval [CI] [-0.37, 0.20]; $I^2 = 0\%$) or hypertrophy (4 studies; SMD = 0.31, 95% CI [-0.14, 0.77]; $I^2 = 0\%$); the imprecision of the hypertrophy estimate means that a modest benefit cannot be excluded. Muscular endurance favoured nutritional intervention (5 studies; SMD = 0.90, 95% CI [0.55, 1.25]; $I^2 = 0\%$), although supplements, exposure periods, and fatigue tasks differed. A qualitative appraisal found no direct study with high methodological confidence; most were small, short, male-dominant, or task-specific. Protein and collagen have not yet demonstrated BFR-specific anabolic synergy when habitual intake is adequate. Creatine, beta-alanine, and betaine remain plausible work-capacity adjuncts, but direct evidence is sparse and inconsistent. Caffeine has task-specific endurance and force-control signals. Nitrate has the most coherent BFR-specific rationale and the broadest fatigue-related pattern, but its apparent advantage remains low precision and has not established a supplement-by-BFR interaction. Nutrition is therefore more likely to modify work quality, fatigue resistance, or neuromotor performance than to produce a proven additional hypertrophic effect. These conclusions and all practical implications should be regarded as provisional pending adequately powered factorial trials.

Keywords: blood flow restriction; resistance training; nutritional supplementation; protein; creatine; caffeine; dietary nitrate; muscular endurance.

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INTRODUCTION

Low-load BFR-RT occupies a distinctive position between conventional low-load and high-load resistance exercise. Across meta-analyses, it generally produces greater muscle growth than low-load free-flow training and broadly similar hypertrophy to high-load training, whereas maximal strength more often favours high-load exercise (Chang et al., 2023; Geng et al., 2024; Ma et al., 2024). This asymmetry is physiologically coherent: BFR accelerates fatigue and motor-unit recruitment at low external loads, but it does not fully reproduce the neural, tendon, and task-specific demands imposed by heavy loading. In athletes, the literature is less uniform. One broad meta-analysis reported improvements across strength, power, speed, endurance, and body-composition outcomes (Yang et al., 2024), whereas a more restrictive lower-limb analysis found only a small strength advantage and no clear superiority for hypertrophy, sprinting, or jumping (Deng et al., 2025). BFR efficacy is therefore not a single property; it varies with the comparator, pressure prescription, exercise mode, test specificity, population, and outcome.

The nutritional question is similarly conditional. It is not whether a supplement is ergogenic in isolation, but whether it addresses a process that remains limiting after the BFR protocol, training dose, habitual diet, and recovery conditions are adequate. Reduced oxygen availability and venous return accelerate metabolite accumulation, discomfort, and task failure. These responses can reduce completed work, alter motor-unit behaviour, and increase the relative importance of phosphagen recovery, buffering, contractile efficiency, and central drive. Conversely, if BFR already recruits and fatigues a sufficient proportion of fibres and the participant consumes adequate energy and protein, an additional anabolic supplement may have little opportunity to increase growth. The same adjunct could still improve repetitions, force control, or performance under fatigue without changing maximal strength or muscle size.

This review proposes a constraint-relief framework to organize that conditional question. The framework separates biological plausibility from demonstrated interaction, target engagement from meaningful performance, acute surrogate responses from chronic adaptation, and general resistance-exercise evidence from direct BFR evidence. Importantly, it is a conceptual heuristic developed from the reviewed patterns; it has not been prospectively validated, and the included studies were not designed to test it as a model. Its purpose is to generate falsifiable questions: Is a proposed constraint present, does the adjunct modify it, and does that modification mediate an outcome that matters?

The review extends the 2026 systematic review and meta-analysis by Zhao and Zhai (2026) in four ways. First, it provides a transparent map of how the focused 28-publication evidence set was selected and prioritized. Second, it adds a study-level qualitative appraisal and applies the same standards of directness, consistency, precision, and duration across supplement classes. Third, it updates the evidence through August 2026 with recent chronic nitrate trials (Yang et al., 2025; Yang et al., 2026) while retaining conservative uncertainty language. Fourth, it connects each evidence section to a remaining constraint and prioritizes factorial designs capable of testing true BFR-nutrition interaction. The central argument is deliberately provisional: current evidence is more compatible with fatigue-resistance and neuromotor signals than with a demonstrated additional effect on hypertrophy or maximal strength.

REVIEW METHOD

Search strategy and transparent selection pathway

A targeted literature search was conducted in PubMed/MEDLINE from database inception through 3 August 2026. The search combined terms for blood flow restriction ("*blood flow restriction*," BFR, KAATSU, and

vascular occlusion) with terms for nutrition and supplementation (nutrition, supplement, protein, whey, collagen, creatine, caffeine, nitrate, beetroot, beta-alanine, betaine, and omega-3). Backward and forward citation searching was performed from retained reviews, meta-analyses, and direct trials, with particular attention to the study set and references reported by Zhao and Zhai (2026).

This was an updated critical narrative review, not a registered systematic review. Screening was not duplicated independently, a formal PRISMA record was not created prospectively, and no claim of exhaustive retrieval is made. Consequently, retrospective counts of all records identified and excluded were not reconstructed. Instead, Figure 1 reports the selection logic, final evidence strata, and prioritization rules without implying a level of systematic-review reproducibility that the design cannot support.

Direct evidence was eligible when an adult human study compared a quantified nutritional intervention combined with BFR or an occlusion-based exercise protocol against BFR alone or BFR plus placebo and reported an objective strength, muscular-endurance, muscle-morphology, or neuromotor outcome. BFR-context evidence was retained when it directly informed the adaptation that nutrition would need to augment, pressure prescription, safety, or outcome specificity. Indirect nutrition evidence was limited to higher-level syntheses relevant to a proposed limiting process. Animal or in-vitro evidence, unquantified dietary exposure, recovery-only BFR interventions, and articles that did not inform the central question were excluded from primary inference. After deduplication and relevance prioritization, 28 publications were retained. Direct evidence was prioritized over indirect plausibility and overlapping studies within reviews were treated as shared evidence rather than independent replication.

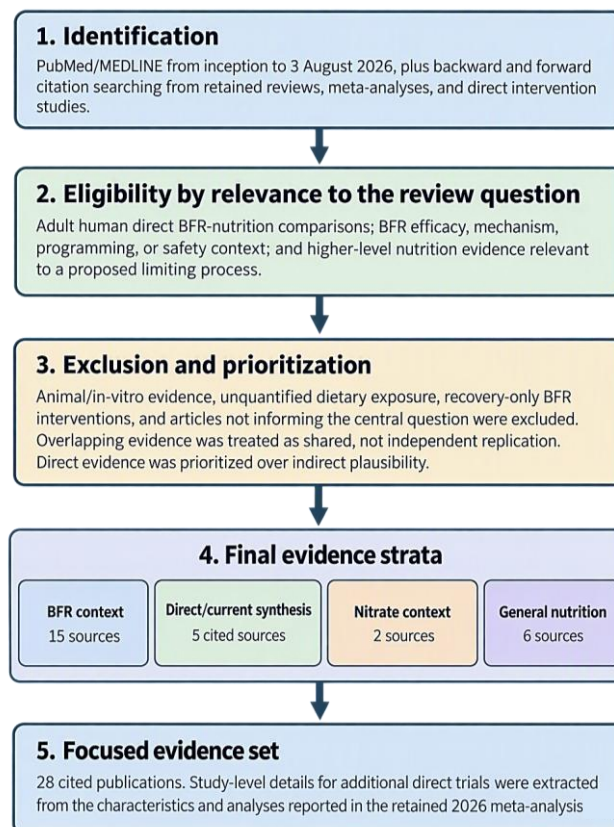


Figure 1. Transparent pathway used to select and prioritize the focused 28-publication evidence set. The diagram reports the final evidence strata without presenting the search as a prospectively documented PRISMA process.

Evidence hierarchy and role of retained publications

Evidence was classified at three inferential levels. First, direct intervention evidence comprised BFR plus nutrition comparisons against BFR alone or placebo, including the nine trials synthesized by Zhao and Zhai (2026), the individually retained caffeine and beta-alanine trials (Lin et al., 2025; Pessoa et al., 2023), and two recent chronic nitrate trials (Yang et al., 2025; Yang et al., 2026). Second, BFR-context evidence defined the strength, hypertrophy, endurance, mechanistic, programming, and safety outcomes that an adjunct would need to improve (Chang et al., 2023; Davis et al., 2024; Deng et al., 2025; Fabero-Garrido et al., 2024; Franz et al., 2023; Geng et al., 2024; He et al., 2025; Ida & Sasaki, 2024; Libardi et al., 2024; Ma et al., 2024; Pignanelli et al., 2023; Reece et al., 2023; Schoenfeld et al., 2023; Wang et al., 2023; Yang et al., 2024). Third, indirect nutrition evidence informed plausibility but could not establish BFR-specific synergy (Antonio et al., 2024; Burke et al., 2023; Casuso & Goossens, 2025; Jahan-Mihan et al., 2025; Poon et al., 2025; Santo Andre et al., 2023; Tan et al., 2023; Therdyothin et al., 2025). Table 1 makes the role and retention logic of each evidence domain explicit.

Table 1. Evidence domains, retention logic, and role of the 28 publications in the critical narrative synthesis.

Evidence domain	References	Retention logic	Role and principal limitation
BFR efficacy and programming	(Chang et al., 2023; Deng et al., 2025; Geng et al., 2024; He et al., 2025; Ma et al., 2024; Yang et al., 2024)	Higher-level syntheses comparing BFR with low- or high-load training and examining pressure or population moderators	Defines comparator-dependent effects and athlete transfer; protocols and subgroups remain heterogeneous.
BFR mechanistic and training studies	(Davis et al., 2024; Ida & Sasaki, 2024; Libardi et al., 2024; Pignanelli et al., 2023; Reece et al., 2023; Schoenfeld et al., 2023)	Human studies or syntheses separating effort, volume, fibre change, signalling, and endurance	Defines candidate constraints and warns against surrogate overinterpretation; samples and durations are small.
Safety and translation	(Fabero-Garrido et al., 2024; Franz et al., 2023; Wang et al., 2023)	Human vascular, thrombotic, or cardiac evidence directly relevant to feasibility	Frames tolerability in screened populations; most evidence is acute or short term.
Direct nutrition plus BFR	(Lin et al., 2025; Pessoa et al., 2023; Yang et al., 2025; Yang et al., 2026; Zhao & Zhai, 2026)	Direct intervention syntheses or primary trials with quantified nutrition and objective outcomes	Provides pooled estimates and study-level signals; evidence is small, short, heterogeneous, and male dominant.
Nitrate and ergogenic context	(Poon et al., 2025; Tan et al., 2023)	Higher-level nitrate evidence aligned with hypoxia, acidosis, repeated effort, power, or velocity	Tests whether the proposed nitrate mechanism is coherent outside BFR; it cannot establish a BFR interaction.
General nutrition context	(Antonio et al., 2024; Burke et al., 2023; Casuso & Goossens, 2025; Jahan-Mihan et al., 2025; Santo Andre et al., 2023; Therdyothin et al., 2025)	Higher-level evidence for creatine, protein, timing, and omega-3	Defines plausibility and general practice; it cannot demonstrate supplement-by-BFR synergy.

Note. BFR, blood flow restriction.

Data extraction and qualitative methodological confidence

Study-level characteristics were organized by design, population, BFR prescription, nutritional exposure, comparator, duration, principal outcome, and interpretive limitation. Conclusions were weighted according to directness, randomization and blinding, adequacy of the BFR comparator, individualization of pressure, nutritional and dietary control, intervention duration, sample size, outcome validity, multiplicity, consistency, and precision. Because several direct trials were available within the characteristics and analyses of Zhao and Zhai (2026) rather than as separately retained primary references, this appraisal was deliberately qualitative and was not presented as a formal Cochrane risk-of-bias or GRADE assessment.

Methodological confidence was classified as follows. High confidence required a well-controlled randomized and blinded comparison, a sufficiently informative sample and duration for the outcome, standardized or individualized BFR, verified nutritional exposure, and a prespecified valid endpoint with limited major concerns. Moderate confidence indicated that several of these features were present but at least one important limitation reduced certainty. Low confidence indicated an acute or very short exposure, small or imbalanced groups, non-training or complete-occlusion tasks, poorly generalizable pressure prescription, exploratory multiplicity, or insufficient control of diet or exposure. These categories describe confidence in an

individual study's design and interpretation; they do not convert a narrative review into a formal certainty assessment.

Quantitative estimates and uncertainty terminology

Pooled SMDs, CIs, study counts, p values, and I² statistics were reproduced from Zhao and Zhai (2026); no new meta-analysis or participant-level recalculation was performed. Non-significant findings were interpreted as an absence of statistically clear evidence, not proof that an effect is zero. Three categories were kept distinct throughout: insufficient evidence, when sparse or imprecise data do not permit a stable conclusion; negative evidence, when estimates favour no benefit or harm but remain uncertain; and evidence supporting no meaningful effect, which would require sufficiently precise estimates to exclude a prespecified important benefit. The current strength and hypertrophy literature generally falls within the first two categories rather than the third.

WHAT REMAINS LIMITING AFTER BFR IS OPTIMIZED?

The outcome must be specified before the constraint

A supplement cannot be judged against a generic label such as “*adaptation*.” Strength measured by 1RM, isometric maximal voluntary contraction, or isokinetic torque is not interchangeable. Endurance measured as repetitions to failure, time to fatigue, total work, torque decay, or performance after fatigue is also not interchangeable. Athlete transfer adds further specificity because sprinting and jumping depend on rapid force production, tendon behaviour, skill, and intermuscular coordination (Deng et al., 2025; Yang et al., 2024). A constraint is therefore meaningful only in relation to a prespecified population, BFR protocol, comparator, and endpoint.

Hypertrophy and maximal strength are partially dissociable

The strongest recurring pattern is that BFR can reproduce much of the hypertrophic effect of heavy training without consistently reproducing its maximal-strength effect (Chang et al., 2023; Geng et al., 2024; Ma et al., 2024). A change in acute signalling or local swelling is not equivalent to additional contractile tissue, and additional muscle size is not guaranteed to improve a high-load 1RM. A nutritional adjunct intended to potentiate BFR must therefore be judged against a defined endpoint rather than an assumed common pathway.

The role of effort is illustrated by Pignanelli et al. (2023). When low-load free-flow and BFR exercise were both performed to task failure within the same participants, AKT and p70S6K responses and six-week hypertrophic adaptations were similar even though the BFR limb completed less work. BFR appeared to accelerate the stress needed to reach a sufficient stimulus rather than demonstrate a higher adaptive ceiling. By contrast, under a volume-matched design, Davis et al. (2024) observed increases in thigh bone-free lean mass and knee-extensor endurance with BFR but not with free-flow training. These studies do not prove that hypertrophy is never limiting; they show that apparent superiority depends on what is matched and that an anabolic adjunct has less room to act when effort, recruitment, energy, and protein are already sufficient.

Fiber-level findings also resist a single anabolic narrative. A systematic review suggested that type I hypertrophy may be at least as large as type II hypertrophy during low-load BFR (Schoenfeld et al., 2023), yet Reece et al. (2023) detected no statistically significant increase in either fibre type after six weeks of BFR in untrained men and women, despite whole-muscle changes comparable with high-load training. Libardi et al. (2024) further showed that early enlargement did not reflect disproportionate expansion of non-myofibrillar

or extracellular compartments. These findings justify uncertainty rather than a claim that one fibre type or compartment is the universal limiting target.

Fatigue, work capacity, and task quality are more plausible modifiable bottlenecks

BFR reliably accelerates local fatigue, but the adaptation depends on the task. Ida and Sasaki (2024) reported similar improvements in maximal strength and muscle thickness with BFR and free-flow training, yet the condition completing more repetitions developed greater repetition-specific endurance. Davis et al. (2024) observed a different pattern under fixed volume: BFR improved total work in a prolonged knee-extensor test, whereas low-load free-flow training showed a signal for improved oxidative capacity. Local endurance can arise from neural, metabolic, muscular, and task-learning adaptations; whether one of these remains limiting depends on the contraction mode, training volume, test, and opportunity to perform additional work.

This domain provides the clearest conditional opportunity for nutrition. Creatine could support phosphocreatine availability, beta-alanine could increase intramuscular buffering, nitrate could influence contractile efficiency under low oxygen and low pH, and caffeine could alter pain, effort perception, or central drive. A plausible mechanism is not sufficient. The relevant process must limit the chosen protocol, the adjunct must modify that process, and the modification must improve meaningful work or function. Fixed repetition schemes can prevent an ergogenic effect from being expressed, whereas sets to failure can reveal additional work but create unequal training exposure.

Protocol quality and safety are prior constraints

Pressure prescription remains central to efficacy and tolerability. Individualized or incrementally adjusted pressure may narrow differences from heavy-load training, and intermittent inflation may be useful in selected protocols (Chang et al., 2023; He et al., 2025). Absolute pressures are difficult to generalize because cuff width, limb circumference, body position, tissue composition, and exercise mode influence the internal stimulus. Nutrition cannot compensate for an excessive, poorly standardized, or poorly tolerated BFR prescription.

Acute venous data in healthy men are reassuring: low-load BFR did not produce greater venous pressure or acute deterioration in venous function than low- or high-load exercise (Franz et al., 2023). Four weeks of low-load BFR in young swimmers improved strength with few detectable changes in left-ventricular structure or function (Wang et al., 2023). Pooled thrombotic biomarkers did not increase in older adults (Fabero-Garrido et al., 2024). These data support supervised use in screened populations but do not establish long-term vascular safety in people with venous disease, cardiovascular comorbidity, or frailty. In clinical translation, screening, pressure individualization, adverse-event monitoring, and exercise feasibility precede any supplement decision.

THE CONSTRAINT-RELIEF FRAMEWORK: A CONCEPTUAL HEURISTIC

Conceptual status and inferential limits

The constraint-relief framework is the central conceptual contribution of this review, but it is not an evidence-validated explanatory system. The retained trials generally compared supplements within BFR conditions; they did not prospectively identify a limiting process, verify target engagement, and test whether its relief mediated chronic adaptation. The framework should therefore be used as a hypothesis-generating decision structure, not as proof that fatigue is always limiting or that hypertrophy is rarely limiting.

Nutritional synergy requires three conditions. First, the adjunct must affect a process that is causally relevant to the intended outcome. Second, that process must remain limiting under the specific BFR protocol, population, habitual diet, and recovery state. Third, the intervention must modify the process enough to change meaningful performance or chronic adaptation rather than only an acute surrogate. Failure at any stage explains why a supplement can be biologically plausible yet produce no clear additional outcome.

Five constraint domains and a prospective causal chain

Five interacting domains organize the candidate constraints. The substrate domain concerns amino-acid and energy availability for remodelling. The energetic domain concerns phosphocreatine recovery, glycolytic work, and buffering. The vascular-contractile domain concerns nitric-oxide bioavailability, oxygen cost, calcium handling, and reperfusion. The neural domain concerns pain, effort perception, central drive, and motor-unit coordination. The remodelling domain concerns inflammation, membrane biology, and anabolic sensitivity.

These domains are not mutually exclusive, and assigning a supplement to one domain does not establish its efficacy. An adjunct that improves repetitions through neural or contractile effects does not necessarily increase integrated muscle protein synthesis. An intervention that changes a kinase, hormone, or whole-body protein-synthesis signal may not increase muscle size or high-load strength. Figure 2 therefore ends with the causal test required for future validation: demonstrate the constraint, verify target engagement, show meaningful improvement in work or function, and establish that the improvement mediates chronic adaptation.

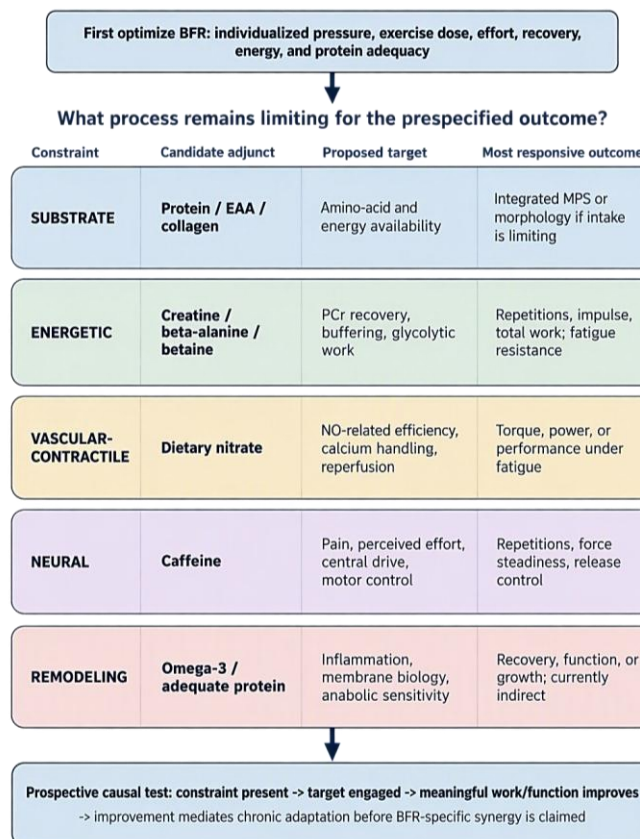


Figure 2. Constraint-relief framework linking five proposed constraint domains to candidate adjuncts, target processes, and outcome classes. The framework is a conceptual heuristic and has not been prospectively validated.

DIRECT EVIDENCE ORGANIZED BY THE REMAINING CONSTRAINT

Pooled evidence and what it does not establish

The 2026 meta-analysis included nine randomized studies and 181 adults (Zhao & Zhai, 2026). Seven studies contributed maximal-strength outcomes, five contributed muscular-endurance outcomes, and four contributed muscle-morphology outcomes. Nutritional interventions did not provide statistically clear average evidence of additional maximal strength (SMD = -0.09, 95% CI [-0.37, 0.20]; $p = .55$; $I^2 = 0\%$) or hypertrophy (SMD = 0.31, 95% CI [-0.14, 0.77]; $p = .18$; $I^2 = 0\%$). Muscular endurance favoured the nutritional condition (SMD = 0.90, 95% CI [0.55, 1.25]; $p < .00001$; $I^2 = 0\%$).

These results do not carry equal inferential meaning. The strength interval is compatible with trivial harm through a small benefit, whereas the hypertrophy interval remains compatible with no effect through a potentially moderate benefit. The endurance estimate is larger and statistically clear, but it combines different supplements, acute and chronic exposure, and non-equivalent fatigue tasks. An I^2 of 0% is not proof of physiological homogeneity when only four to seven small studies contribute. Table 2 therefore uses uncertainty categories rather than treating non-significance as evidence that an effect is absent.

Table 2. Pooled direct evidence and outcome-specific uncertainty.

Outcome	Studies	Pooled SMD	95% CI	p value; I^2	Interpretation
Maximal strength	7	-0.09	[-0.37, 0.20]	.55; 0%	No statistically clear average benefit; the interval includes trivial harm and a small benefit. It does not prove equivalence.
Muscular endurance	5	0.90	[0.55, 1.25]	<.00001; 0%	Favourable pooled signal, but certainty is limited by heterogeneous supplements, exposures, and tasks.
Muscle hypertrophy/morphology	4	0.31	[-0.14, 0.77]	.18; 0%	Insufficient and imprecise evidence; no clear average effect, but a modest benefit cannot be excluded.

Note. Pooled estimates are reproduced from Zhao and Zhai (2026). These interpretations are qualitative and are not formal GRADE ratings. CI, confidence interval; SMD, standardized mean difference.

Study-level methodological appraisal

No direct trial met the criteria for high methodological confidence. Moderate ratings reflected relatively stronger randomization, blinding, individualized pressure, or chronic exposure, but all retained important limitations. Low ratings were driven by acute or very short exposure, non-training or complete-occlusion tasks, small or imbalanced samples, limited pressure generalizability, or exploratory multiplicity. The ratings in Table 3 should contextualize, not replace, a formal risk-of-bias assessment.

Table 3. Study-level map and qualitative methodological confidence for direct nutritional interventions combined with BFR or occlusion-based exercise.

Study/source	Design and intervention	Principal signal	Key limitation	Confidence
Hoon et al. (2015), summarized in Zhao and Zhai (2026)	Acute double-blind trial; 18 healthy participants; electrically stimulated knee extension under 250 mmHg occlusion; nitrate for 3 days plus test-day dose	Improved fatigue resistance; no basis for chronic adaptation inference	Electrical stimulation and absolute occlusion pressure limit training translation	Low
Souza et al. (2018), summarized in Zhao and Zhai (2026)	Acute trial; 22 trained adults; unilateral knee extension to failure at 30% 1RM and 80% AOP; caffeine 6 mg/kg	More repetitions under BFR; perceptual and metabolic outcomes also measured	Single bout, small sample, and low habitual caffeine exposure	Low
Papadopoulos et al. (2018), summarized in Zhao and Zhai (2026)	Acute trial; 16 young male participants; sustained handgrip at 30% MVC with 250 mmHg occlusion; nitrate 8.1 mmol	Longer time to fatigue	Upper-limb isometric task and complete arterial occlusion; no chronic inference	Low
Centner et al. (2019), summarized in Zhao and Zhai (2026)	Double-blind chronic trial; 22 older untrained men; leg press at 20-30% 1RM and 50% AOP; collagen hydrolysate 15 g/day	No clear added 1RM or cross-sectional-area effect	Small male sample; collagen is not equivalent to a leucine-rich complete protein	Moderate
Machek et al. (2022), summarized in Zhao and Zhai (2026)	Double-blind short-loading trial; 18 recreationally trained adults; unilateral leg press at 20% 1RM and 80% AOP; betaine 6 g/day	Contributed to the pooled endurance signal	Short exposure, small sample, and multiple exploratory biomarkers	Low

Sousa-Silva et al. (2023), summarized in Zhao and Zhai (2026)	Double-blind trial; 17 healthy men; 8 weeks; biceps curl at 30% 1RM and 50% AOP; creatine loading then 5 g/day	Possible muscle-thickness and low-load endurance benefits; no clear added maximal-strength effect	Small unilateral mixed design; early thickness changes may reflect hydration	Moderate
Pessoa et al. (2023)	Randomized double-blind trial; 19 untrained adults; 6 weeks; biceps curl at 30% 1RM and 50% AOP; beta-alanine 4.8 g/day	No added 1RM or cumulative-work benefit	Small single-joint model; buffering may not have been the limiting process	Moderate
Lin et al. (2025)	Randomized trial; 28 untrained adults; 4 weeks; wrist-extension BFR at 20% MVC; caffeine 6 mg/kg before training	No added maximal-force gain; improved force-release control and motor-unit behaviour	Task-specific isometric model, surface-EMG decomposition, and nonhabitual users	Moderate
Vendruscolo et al. (2025), summarized in Zhao and Zhai (2026)	Chronic trial; 21 resistance-trained men; 3 weeks; biceps curl at 30% 1RM and 80% AOP; whey protein 25 g twice daily	Some strength and regional hypertrophy signals; pooled evidence remained inconclusive	Very short duration, small placebo group, multiple regional outcomes, and adequate baseline protein	Low
Yang et al. (2025)	Randomized chronic trial; 21 male college athletes; 4 weeks; isokinetic lower-limb BFR; beetroot juice with 8 mmol nitrate/day	Greater preservation of torque and power during later fatigue phases	Small male sample; fatigue performance was more responsive than maximal strength	Moderate
Yang et al. (2026)	Randomized double-blind trial; 20 male students; 4 weeks; bilateral knee BFR at 40% limb occlusion pressure and 30% peak torque; beetroot juice 8 mmol/day	Selective improvement in fatigued bilateral jump performance	Small sample, short duration, multiple outcomes, and limited generalizability	Moderate

Note. Study-level details for trials not separately included in the 28-reference list were extracted from the characteristics and analyses reported in Zhao and Zhai (2026). Confidence is qualitative, not a formal risk-of-bias rating. 1RM, one-repetition maximum; AOP, arterial occlusion pressure; MVC, maximal voluntary contraction.

Substrate and remodelling constraints: protein, collagen, and omega-3

Protein is the most intuitive anabolic adjunct, but the relevant constraint is dietary insufficiency, not the presence of a cuff. General athlete evidence indicates that supplementation is most useful when habitual intake is insufficient; benefits diminish when total intake, meal distribution, and essential amino-acid availability are already adequate (Antonio et al., 2024; Jahan-Mihan et al., 2025). Direct comparisons of pre-versus post-exercise ingestion show no meaningful difference in lean-mass adaptation, arguing against an exceptionally narrow anabolic window (Casuso & Goossens, 2025).

The BFR evidence is mixed and imprecise. A three-week whey-protein trial in resistance-trained men reported greater absolute 1RM gains and some site-specific cross-sectional-area signals, but the short duration, small placebo group, adequate baseline protein intake, and multiple regional measurements limit confidence (Zhao & Zhai, 2026). The collagen trial in older men did not establish an additional strength or muscle-size effect (Zhao & Zhai, 2026). These findings are insufficient to demonstrate BFR-specific anabolic synergy, but they do not establish that protein could never help a participant with low intake or anabolic resistance. The testable prediction is an interaction with baseline substrate limitation, not a universal timing effect.

Omega-3 fatty acids occupy the remodelling domain, but the retained evidence is entirely indirect to BFR. A broad meta-analysis reported small, uncertain, and heterogeneous effects on strength, muscle mass, and function (Santo Andre et al., 2023). A protein-synthesis meta-analysis found no increase in muscle protein synthesis, although whole-body protein synthesis increased (Therdyothin et al., 2025). Whole-body synthesis includes non-muscle tissues and cannot be assumed to translate into hypertrophy. Without a direct omega-3 plus BFR comparison, a BFR-specific remodelling claim is unsupported.

Energetic constraints: creatine, beta-alanine, and betaine

Creatine has a stronger general resistance-training evidence base than most candidates considered here. A meta-analysis using regional imaging reported a very small hypertrophy advantage when creatine was combined with resistance training, with uncertainty extending toward trivial effects (Burke et al., 2023). The

BFR rationale is plausible because greater intramuscular creatine availability could support phosphocreatine resynthesis and repeated contractions when recovery is constrained. The direct eight-week trial reported possible muscle-thickness and low-load endurance benefits, but maximal strength was not clearly augmented and early thickness differences were not sustained (Zhao & Zhai, 2026). The evidence is compatible with a work-capacity effect, but it does not establish a specific creatine-by-BFR interaction.

Beta-alanine is mechanistically aligned with repeated acidic exercise because increased muscle carnosine can improve proton buffering. However, the six-week direct trial found no additional 1RM or cumulative-work benefit with BFR or traditional training (Pessoa et al., 2023). This is a negative study, but its small single-joint design is not precise enough to demonstrate that a meaningful effect is absent across BFR protocols. Betaine contributed to the favourable pooled endurance estimate, but the evidence comes from a small, short-loading leg-press study (Zhao & Zhai, 2026). Beta-alanine and betaine should not be treated as interchangeable, and neither is an established BFR adjunct.

The decisive design issue is whether additional capacity can be expressed. Fixed-volume trials may conceal an energetic effect, whereas work-unmatched sets to failure can reveal it but also change the training dose. Future studies should quantify target engagement and report repetitions, time under tension, impulse, volume load, pain, and session rating of perceived exertion, then test whether additional effective work mediates chronic adaptation.

Neural constraints: caffeine

Caffeine targets neural and perceptual constraints more directly than anabolic remodelling. Acute caffeine improved repetitions during a lower-body BFR task in trained participants, contributing to the pooled endurance signal (Zhao & Zhai, 2026). In the four-week wrist-extensor trial, both caffeine and placebo groups increased maximal voluntary contraction, while caffeine modified force-release fluctuations and motor-unit discharge behaviour (Lin et al., 2025). A conventional maximal-force endpoint alone would therefore have missed a task-specific neuromotor signal.

The finding is promising but narrow. The chronic study used a small upper-limb isometric model, low pressure, nonhabitual caffeine users, and surface electromyography decomposition (Lin et al., 2025). Current evidence is insufficient to demonstrate that caffeine adds chronic maximal strength or hypertrophy to BFR. The prospective framework predicts benefit only when pain, perceived effort, endurance, or fine force control is the relevant constraint, and that prediction requires replication in dynamic, larger-muscle, and habitual-use-stratified designs.

Vascular-contractile constraints: dietary nitrate

Nitrate has the most distinctive BFR-specific rationale because reduction of nitrite to nitric oxide is favoured by low oxygen and low pH, conditions intentionally created during BFR. Across broader exercise evidence, nitrate benefits are more consistent for endurance-related outcomes than for maximal strength (Poon et al., 2025). Resistance-exercise evidence suggests small improvements in repetitions to failure and mean power or velocity, but not consistently in peak values (Tan et al., 2023). These indirect findings support plausibility but do not prove a nitrate-by-BFR interaction.

The earlier direct evidence consisted mainly of small acute handgrip or electrically stimulated fatigue protocols and supported fatigue resistance rather than chronic hypertrophy or strength (Zhao & Zhai, 2026). Two recent four-week lower-limb studies extend the pattern (Yang et al., 2025; Yang et al., 2026). Beetroot juice was more likely to preserve torque, power, or jump performance under fatigue than to produce uniform

superiority in maximal strength. This convergence across fatigue-related outcomes is more consistent than the evidence for most other adjuncts, but the same evidential standard still applies: samples were small and male only, interventions were short, protocols were closely related, and precision was limited. Nitrate is therefore the highest-priority candidate for a definitive factorial test, not a proven routine prescription.

Several questions remain unresolved. It is unknown whether nitrate produces a statistically identifiable supplement-by-BFR interaction rather than a general main effect; whether an acute or short-term fatigue benefit increases long-term training adaptation; whether target engagement is mediated mainly by contractile efficiency, calcium handling, reduced oxygen cost, or post-cuff reperfusion; and whether the pattern generalizes to women, older adults, clinical populations, or highly trained athletes. Long-term safety and adherence in supplement-BFR combinations also remain insufficiently characterized.

Applying one evidential standard across supplement classes

Table 4 compares supplement classes using the same dimensions: directness, consistency, precision, most responsive outcome, and current interpretation. No class has high-certainty evidence for BFR-specific synergy. Nitrate has the broadest direct fatigue-related pattern, caffeine has a narrower endurance and motor-control pattern, and protein-class, creatine, beta-alanine, betaine, and omega-3 evidence remains insufficient or indirect for the claimed interaction.

Table 4. Cross-supplement comparison using a common evidential standard.

Adjunct/class	Direct BFR evidence	Consistency and precision	Most responsive outcome	Current interpretation
Protein/collagen	Small chronic whey and collagen trials plus pooled morphology/strength estimates (Zhao & Zhai, 2026)	Mixed findings; short durations and imprecise pooled morphology estimate	Dietary adequacy; morphology or strength if substrate limited	Insufficient to demonstrate BFR-specific anabolic synergy; supplementation remains appropriate when it corrects inadequate intake.
Creatine	One small eight-week direct trial summarized in Zhao and Zhai (2026)	Possible thickness/endurance signals; no clear maximal-strength effect; low precision	Repeated work or low-load endurance	Plausible energetic adjunct with general merits, but no demonstrated creatine-by-BFR interaction.
Beta-alanine	One small six-week trial (Pessoa et al., 2023)	Null 1RM and cumulative-work findings; too sparse to establish absence of effect	Buffering-dependent repeated work	Insufficient evidence; the tested protocol may not have been buffering limited.
Betaine	One small, short-loading trial summarized in Zhao and Zhai (2026)	Favourable endurance contribution but isolated and imprecise	Work capacity/endurance	Hypothesis generating only.
Caffeine	One acute trial summarized in Zhao and Zhai (2026) and one four-week trial (Lin et al., 2025)	Repetition and motor-control signals; no clear additional maximal force; task specific	Repetitions, effort tolerance, force control	Promising when neural or perceptual constraints are present; chronic transfer remains uncertain.
Dietary nitrate	Two acute fatigue studies summarized in Zhao and Zhai (2026) and two short chronic trials (Yang et al., 2025; Yang et al., 2026)	Most consistent fatigue-related pattern, but small male samples and limited independent replication	Torque, power, or performance under fatigue	Highest-priority candidate for a factorial test; not established as a routine BFR adjunct.
Omega-3	No direct BFR trial; indirect syntheses only (Santo Andre et al., 2023; Therdyothin et al., 2025)	Heterogeneous general outcomes and no clear muscle-protein-synthesis effect	Remodelling or function, if relevant	No BFR-specific inference is currently justified.

INTEGRATED MECHANISTIC INTERPRETATION

Constraint presence must be demonstrated

The first step is not choosing a supplement but demonstrating that its target is limiting. Adequate habitual protein weakens the rationale for additional substrate; fixed repetitions weaken the opportunity for a work-capacity adjunct; low pain or effort weakens the neural rationale; and excessive cuff pressure can dominate

all nutritional effects. Baseline diet, training status, habitual caffeine use, pressure, exercise dose, and outcome demand should therefore be prespecified moderators rather than post hoc explanations.

Target engagement is not equivalent to meaningful adaptation

BFR can elicit mTORC1-associated signalling and other anabolic responses, but effort-matched data show that these responses are not necessarily greater once low-load exercise reaches task failure (Pignanelli et al., 2023). Early AKT-mTOR phosphorylation did not reliably predict subsequent hypertrophy in the effort-matched study (Pignanelli et al., 2023). Acute lactate, growth hormone, insulin-like growth factor-1, cell swelling, or kinase phosphorylation can demonstrate that a stimulus occurred, but they do not independently establish chronic muscle growth. Similarly, whole-body protein synthesis, dual-energy X-ray absorptiometry, muscle thickness, biopsy samples, and functional outcomes can diverge (Davis et al., 2024; Libardi et al., 2024; Pignanelli et al., 2023; Reece et al., 2023; Therdyothin et al., 2025). Target engagement should therefore be measured, but it should not substitute for the prespecified structural or functional endpoint.

Additional work is a mediator, not automatically a benefit

Creatine, beta-alanine, betaine, nitrate, and caffeine are most likely to matter when greater energetic, contractile, or neural capacity can be converted into additional high-quality work. That additional work could plausibly improve chronic adaptation, but it could also increase discomfort, recovery demand, or dose heterogeneity. A valid causal chain requires mediation analysis: the adjunct changes a target, the target change increases effective work or task quality, and that increase explains a chronic outcome. Without this chain, an acute ergogenic response should not be labelled BFR-specific synergy.

Nitric oxide and motor control illustrate outcome specificity

Although hypoxia and acidosis favour nitric-oxide generation (Poon et al., 2025; Tan et al., 2023), cuff pressure limits the ability of vasodilation to increase bulk flow during exercise. Nitrate benefits may therefore emerge through contractile efficiency, calcium handling, reduced oxygen cost, or reperfusion after cuff release. This predicts stronger effects on repeated effort and performance under fatigue than on maximal voluntary strength, consistent with the emerging direct pattern (Yang et al., 2025; Yang et al., 2026; Zhao & Zhai, 2026). The caffeine trial makes a parallel point: a supplement can modify force-release control and motor-unit behaviour without increasing maximal force (Lin et al., 2025). These are potentially meaningful signals, but they remain task-specific until reproduced in outcomes that matter to rehabilitation or sport.

CRITICAL DISCUSSION AND BROADER IMPLICATIONS

Principal synthesis

The principal finding is a mismatch between mechanistic richness and evidential depth. Nearly every supplement considered has a plausible pathway, yet the direct evidence is small, short, and heterogeneous. The only pooled outcome with a statistically clear favourable estimate is muscular endurance (Zhao & Zhai, 2026), and recent nitrate trials primarily strengthen a fatigue-related interpretation (Yang et al., 2025; Yang et al., 2026). Strength and hypertrophy estimates do not demonstrate a clear additional average benefit, but their precision is not sufficient to claim that all meaningful benefit is absent.

The constraint-relief heuristic offers one coherent interpretation without claiming validation. BFR can create an efficient low-load stimulus, potentially leaving less opportunity for an anabolic adjunct when diet and effort are adequate, while simultaneously creating discomfort and fatigue that an ergogenic adjunct might relieve. This remains a hypothesis. The existing studies generally did not identify the limiting constraint before intervention or test whether relief of that constraint mediated adaptation.

Outcome selection can reverse apparent efficacy. Broad pooling may create an impression of general performance enhancement that disappears when the comparator and test are narrowed (Deng et al., 2025; Yang et al., 2024). The literature is also vulnerable to surrogate overinterpretation and selective emphasis. High-quality research should treat disagreement among molecular, microscopic, imaging, and functional outcomes as a biological and measurement question rather than selecting the endpoint that best supports synergy.

Process-based sports nutrition beyond BFR

Most supplementation reviews are organized around ingredients. The present framework instead begins with a limiting process and asks whether an intervention relieves it. As a conceptual approach, this logic could extend beyond BFR to other training settings in which the same ingredient may be useful or irrelevant depending on the task, baseline diet, recovery state, and performance bottleneck. The transferable contribution is not a universal list of supplements; it is the sequence of questions: define the outcome, identify the constraint, verify target engagement, and test whether relief changes meaningful function or adaptation. Application outside BFR should also be regarded as hypothesis generating until evaluated prospectively.

Generalizability

The direct literature is dominated by young men, small samples, upper-limb single-joint tasks, and interventions lasting eight weeks or less. Women, older adults, clinical populations, and highly trained athletes remain underrepresented. Existing older-adult biomarker and safety evidence supports cautious supervised use but does not establish that a supplement improves clinical function or long-term safety (Fabero-Garrido et al., 2024; Franz et al., 2023; Wang et al., 2023). Population-specific constraints should therefore be stated as testable hypotheses rather than assumed from young healthy samples.

STRENGTHS AND LIMITATIONS OF THE REVIEW

This review applies an explicit outcome-specific framework, separates direct from indirect evidence, reports pooled estimates with CIs and study counts, adds a transparent selection pathway, provides a qualitative methodological appraisal, and applies common evidential standards across supplement classes. It also updates nitrate evidence beyond the search window of the retained 2026 meta-analysis and converts mechanistic claims into prioritized, testable designs. Organizing the synthesis around remaining constraints keeps the conceptual contribution visible while preserving study-level detail.

The limitations are substantial. This is a targeted critical narrative review rather than a registered systematic review. Screening and extraction were not duplicated independently, initial search and exclusion counts were not documented prospectively, and formal risk-of-bias and GRADE procedures were not undertaken. The selection pathway improves transparency but does not make the evidence set exhaustive. The 28 publications were deliberately focused, and several direct trials were appraised through study-level information reported in Zhao and Zhai (2026) rather than through separate inclusion of every primary article in the reference list. The qualitative confidence categories are interpretive and may not capture every domain-specific bias.

The pooled estimates combine different supplements, populations, BFR prescriptions, exposure periods, and endpoints. Low I^2 values are not reassuring when only a few small studies contribute, and publication bias cannot be reliably excluded. The recent nitrate trials are short, male only, and methodologically related, so they do not establish long-term efficacy, safety, or broad independent replication (Yang et al., 2025; Yang et al., 2026). Finally, the constraint-relief framework was derived as a conceptual heuristic from the observed

literature; it has not been prospectively tested. These limitations require conservative and explicitly provisional conclusions.

PROVISIONAL PRACTICAL AND TRANSLATIONAL IMPLICATIONS

The following implications are provisional interpretations of limited evidence, not established best-practice guidelines. They should not override clinical screening, dietary assessment, individualized exercise programming, or professional judgment.

A constraint-first decision sequence

1. Define the target outcome: heavy-load strength, low-load hypertrophy, repetitions, fatigue resistance, force control, rehabilitation tolerance, or sport transfer.
2. Optimize the BFR prescription and report cuff width, individualized arterial or limb occlusion pressure, body position, inflation pattern, load, repetitions, rest, and proximity to failure.
3. Assess baseline constraints, including energy and protein intake, training status, habitual supplement exposure, pain, task tolerance, and recovery.
4. Select an adjunct only when its proposed target plausibly remains limiting.
5. Monitor target engagement, work quality, adverse events, and the prespecified outcome; do not infer chronic benefit from a single surrogate.

Population-specific hypotheses

The constraint most likely to remain after BFR optimization may differ by population. Table 5 separates hypotheses from recommendations and highlights the limits of current evidence.

Table 5. Population-specific constraint hypotheses and provisional translational implications.

Population	Potential remaining constraint	Priority outcome	Provisional implication	Evidence caveat
Resistance-trained athletes	Task-specific work quality, fatigue resistance, power transfer, or heavy-load specificity	Repetitions, torque/power under fatigue, sprint/jump transfer, high-load strength	Nitrate or caffeine may warrant research when fatigue or neural constraints are documented; heavy-load exposure remains important for maximal strength	Direct studies are small, male dominant, and short; athlete transfer is inconsistent (Deng et al., 2025; Yang et al., 2024; Yang et al., 2025; Yang et al., 2026).
Untrained or recreational adults	Tolerance, motor learning, and basic work capacity	Adherence, repetitions, strength, and morphology	Dietary adequacy and protocol quality should precede supplementation; energetic adjuncts remain unconfirmed	Many direct studies use small single-joint models (Lin et al., 2025; Pessoa et al., 2023; Zhao & Zhai, 2026).
Older adults	Anabolic resistance, low dietary intake, functional capacity, and tolerability	Function, strength, muscle size, safety, and adherence	Protein may be relevant when intake or anabolic responsiveness is low; this interaction has not been demonstrated within BFR	Direct supplementation and long-term safety evidence are limited (Fabero-Garrido et al., 2024; Franz et al., 2023; Wang et al., 2023; Zhao & Zhai, 2026).
Rehabilitation or clinical populations	Pain, load intolerance, comorbidity, movement quality, and safety	Functional task performance, force control, symptoms, adverse events	Screening, supervision, pressure individualization, and function take precedence; no routine BFR supplement strategy is established	High-risk populations are underrepresented and long-term combination safety is unknown (Fabero-Garrido et al., 2024; Franz et al., 2023; Wang et al., 2023).

Outcome-specific provisional interpretations

- *Maximal strength*: no adjunct has demonstrated a clear average additive BFR effect. When clinically permissible, progressive exposure to the load and task being tested remains the more direct strategy.
- *Hypertrophy*: current evidence is insufficient to show reliable additional growth, but imprecision means a modest benefit cannot be excluded. Energy, protein adequacy, progression, and effort remain the primary modifiable factors.
- *Repeated-effort performance*: nitrate, caffeine, creatine, betaine, and buffering strategies are mechanistically relevant, but evidence is outcome specific and generally low precision.

- *Force control or performance under fatigue:* caffeine and nitrate have promising task-specific signals; transfer to broader sport or clinical tasks remains uncertain.
- *Low protein intake or anabolic resistance:* protein supplementation is defensible when it corrects a documented dietary constraint, not because BFR creates a proven unique anabolic window. General athlete guidance supports approximately 1.2-2.0 g/kg/day distributed across meals of roughly 0.25-0.40 g/kg, depending on training and clinical context (Jahan-Mihan et al., 2025), and precise pre-versus post-exercise timing is unlikely to determine adaptation (Casuso & Goossens, 2025).

What cannot yet be recommended

The evidence does not justify a universal multi-ingredient BFR stack, a claim that nitrate overcomes cuff-induced ischemia, a unique BFR anabolic window for protein, or the use of acute anabolic hormones as predictors of chronic hypertrophy. It also does not establish long-term vascular safety of supplement-BFR combinations in high-risk clinical populations. Nitrate should be presented as a research priority, not a proven standard supplement for BFR.

PRIORITIZED FUTURE RESEARCH DIRECTIONS

The next generation of studies should estimate an interaction rather than merely demonstrate that BFR and a supplement can each work. A 2 x 2 factorial design - BFR versus free flow and supplement versus placebo - can separate the main effects of training and supplementation from synergy. A high-load comparator can be added as a prespecified reference arm when clinically relevant. BFR should be standardized through individualized pressure, cuff width, body position, inflation continuity, load, repetition target, interset rest, and proximity to failure. Diet should be quantified and supplement exposure verified through adherence measures or biomarkers.

Mechanistic and chronic outcomes should be linked in the same participants. Priority measurements include integrated myofibrillar protein synthesis, mTORC1 signalling at multiple time points, phosphocreatine recovery, muscle pH, oxygenation, perfusion, mitochondrial function, motor-unit behaviour, magnetic resonance imaging or panoramic ultrasound, strength across matched and unmatched tests, and task-specific endurance. Interventions intended to establish chronic adaptation should generally extend beyond 12 weeks, with follow-up for retention and adverse events. Table 6 ranks the most informative experiments by expected scientific value and translational relevance.

Table 6. Prioritized experiments for testing the constraint-relief framework.

Priority	Question and preferred design	Key measurements	Decisive interpretation	Why prioritized
1	Does nitrate produce chronic BFR-specific synergy? A 12-16 week nitrate/placebo x BFR/free-flow factorial trial	Plasma nitrate/nitrite, oxygenation, phosphocreatine recovery, repetitions, imaging, strength, and fatigue performance	A prespecified nitrate x BFR interaction is required; mediation should test whether improved training quality explains adaptation	Strongest direct fatigue-related pattern but no definitive interaction test (Yang et al., 2025; Yang et al., 2026; Zhao & Zhai, 2026)
2	Do creatine or beta-alanine increase effective work? Work-unmatched sets to failure followed by a chronic factorial phase	Phosphocreatine recovery or muscle carnosine, pH, impulse, volume, endurance, and chronic outcomes	Target engagement and additional work should mediate adaptation if the mechanism is causal	Resolves whether fixed-volume designs conceal an energetic effect (Pessoa et al., 2023; Zhao & Zhai, 2026)
3	Does caffeine improve meaningful movement quality? Habitual-use-stratified dynamic BFR trial	Pain, perceived exertion, force steadiness, braking, motor units, task skill, and safety	A reproducible functional or neuromotor benefit can be meaningful even without greater maximal strength	Extends a promising but narrow task-specific signal (Lin et al., 2025)
4	Does protein help when substrate availability is genuinely limiting? Recruit or stratify low-intake or anabolic-resistant participants and control total intake	Dietary intake, integrated muscle protein synthesis, muscle size, strength, and function	Benefit should be larger in low-intake or anabolic-resistant strata than in already adequate participants	Directly tests the framework instead of assuming a universal anabolic window (Antonio et al., 2024; Casuso & Goossens, 2025; Jahan-Mihan et al., 2025; Zhao & Zhai, 2026)

5	Which populations and phenotypes respond? Large multisite trial including women, older adults, clinical participants, and trained athletes	Baseline phenotype, pressure, diet, sex, training status, individual responses, and task transfer	Prespecified moderators should explain heterogeneity without post hoc responder labels	Addresses the major generalizability gap
6	Are supplement-BFR combinations safe over the long term? Prospective study lasting at least 6 months in screened populations	Adverse events, vascular function, thrombotic markers, adherence, and clinical function	Safety inference requires event reporting and functional vascular outcomes, not biomarkers alone	Essential for rehabilitation, older adults, and clinical translation (Fabero-Garrido et al., 2024; Franz et al., 2023; Wang et al., 2023)

CONCLUSIONS

Nutrition does not automatically amplify BFR-RT. Current pooled evidence does not provide statistically clear average evidence of additional maximal strength or hypertrophy, but the small and imprecise hypertrophy literature cannot exclude a modest benefit. Muscular endurance and performance under fatigue are more promising, although certainty is limited by heterogeneous supplements, tasks, and short male-dominant studies. Protein should be used to correct documented dietary insufficiency rather than exploit an unproven BFR-specific anabolic window. Creatine, beta-alanine, betaine, and omega-3 fatty acids remain plausible but unconfirmed BFR adjuncts. Caffeine has task-specific endurance and force-control signals. Nitrate has the most coherent and comparatively consistent fatigue-related evidence, but it has not established a nitrate-by-BFR interaction or a routine prescription.

The constraint-relief framework should be understood as a conceptual heuristic, not a validated explanatory model. Its value lies in replacing ingredient-first reasoning with a prospective causal sequence: identify the outcome, demonstrate the remaining constraint, verify target engagement, and test whether relief improves meaningful work or function and mediates chronic adaptation. Until factorial trials complete that sequence, optimized BFR prescription, adequate habitual nutrition, population-specific screening, and outcome-specific exercise programming are more defensible than any universal supplement strategy.

AUTHOR CONTRIBUTIONS

All authors meet the criteria for authorship in accordance with established ethical guidelines. Contributions are specified according to the CRediT (Contributor Roles Taxonomy) as follows:

Conceptualisation: Aida Mohammadi, Parham Jalali, Goran Sporiš, Hadi Nobari. Methodology: Aida Mohammadi, Tolga Tek, Parham Jalali. Formal analysis: Not applicable in this review article; no new formal statistical analysis was performed. Investigation: Aida Mohammadi, Tolga Tek, Parham Jalali, Benyamin Asadi, Ivica Franjko, Kaja Gutenberger. Data curation: Aida Mohammadi, Parham Jalali, Benyamin Asadi, Kaja Gutenberger. Writing – original draft: Aida Mohammadi, Tolga Tek, Parham Jalali. Writing – review & editing: Aida Mohammadi, Tolga Tek, Parham Jalali, Benyamin Asadi, Ivica Franjko, Goran Sporiš, Kaja Gutenberger, Hadi Nobari. Supervision: Goran Sporiš, Hadi Nobari.

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