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Biochemical markers of muscle damage and recovery: Insights from exercise physiology and molecular biology

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ABSTRACT

Exercise-induced muscle damage (EIMD) is a multifactorial biological phenomenon arising from the coordinated effects of mechanical overload, metabolic perturbations, oxidative stress, inflammatory signaling, and molecular remodeling. Rather than constituting a purely deleterious consequence of exercise, EIMD represents a dynamic physiological stimulus that initiates repair, regeneration, and long-term skeletal muscle adaptation. This review synthesizes current evidence to provide an integrated framework linking structural disruption at the sarcomeric level with downstream biochemical responses, immune regulation, and growth factor–mediated remodeling processes. Classical biochemical markers, including creatine kinase, lactate dehydrogenase, and myoglobin, remain widely used indicators of sarcolemmal permeability and metabolic stress; however, their interpretative value is limited by indirectness and substantial inter-individual variability. Emerging structural biomarkers such as skeletal muscle troponins, titin fragments, and desmin offer enhanced mechanistic specificity by directly reflecting myofibrillar and cytoskeletal disruption, thereby improving the molecular resolution of EIMD assessment. Concurrently, tightly regulated inflammatory responses characterized by a temporal transition from pro-inflammatory to anti-inflammatory signaling play a dual role by mediating tissue clearance while promoting satellite cell activation and regenerative remodeling. Growth factors including insulin-like growth factor-1, fibroblast growth factor-2, vascular endothelial growth factor, and the inhibitory regulator myostatin are highlighted as central integrators of mechanical, metabolic, and immune-derived cues that coordinate myogenesis, angiogenesis, and hypertrophic adaptation. From a practical perspective, the review emphasizes that optimal management of EIMD should focus on modulation rather than suppression of damage-associated pathways through appropriate exercise prescription, nutritional support, and recovery strategies. Collectively, EIMD is conceptualized as a programmable biological process whose magnitude, timing, and resolution critically determine skeletal muscle resilience, performance, and long-term health.

1. Introduction

Skeletal muscle is one of the most metabolically active and structurally complex tissues in the human body, which is involved in locomotion, thermogenesis, metabolic regulation and the overall functional ability (Feng et al., 2024; Wang et al., 2025). It is both structurally unconventional, with multinucleated fibers that are wrapped in the sarcolemma, sarcomeres that are organized in a detailed fashion, and a robust cytoskeletal scaffold, which provides it with impressive force-generating abilities, as well as a natural susceptibility to mechanical and metabolic stressors (Zhao et al., 2025). The mechanical load on myofibrils during a demanding or unfamiliar physical exercise, particularly eccentric loading, causes sarcomere alignment perturbations, Z -disk streaming, excitation -contraction coupling perturbation, and membrane integrity breakage (Chatzinikita et al., 2025). An initial set of ultrastructural events trigger a cascade of biochemical and inflammatory events known as exercise-induced muscle damage (EIMD) that is a widely researched but not fully understood phenomenon in its molecular complexity (Li et al., 2024).

The triumvirate of EIMD pathophysiology includes mechanical overload and metabolic fatigue as well as oxidative stress (Schwiete et al., 2025). Mechanical strain is also broadly considered the main

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cause of sarcomeric disruption, especially in eccentric contraction whereby non-uniform lengthening of the myofibrils results in focal microtears (Kamal and Trombetta-Lima, 2025). In addition to this mechanical factor, metabolic fatigue, which is marked by ATP depletion, ion imbalance, and inorganic phosphate buildup, reduces the load-resistance of the muscle, decreases the structural failure threshold, and activates calcium-dependent proteolytic pathways (Hendry et al., 2025). Oxidative stress also increases the damage by overproduction of reactive oxygen species (ROS) by mitochondria, NADPH oxidases, and infiltrating immune cells, which add to lipid peroxidation, protein oxidation, and mitochondrial dysfunction (Özdemir and Demir, 2025). Interestingly, these processes do not work in isolation but constitute a complex web of biomechanical and biochemical interactions which determine acute reactions as well as long-term changes to exercise stress. Clinically, such processes of the multifactorial damage present as delayed-onset muscle soreness (DOMS), temporary loss of force production, heightened muscle stiffness, and delayed recovery requirements (Sonkodi, 2025). These combined, interconnected systems of biomechanical and biochemical functions are what give rise to the acute symptoms of EIMD, which include delayed/onset muscle soreness, and transient force loss and at the same time, serve as the sources of molecular stimuli to facilitate subsequent repair, remodeling and strengthening of skeletal muscle (Matthews et al., 2024; Bolger et al., 2025).

Despite the large amount of literature that has focused on the functional outcomes and histological characteristics of exercise induced muscle damage, biochemical markers are vital in the measurement of the extent and temporal changes of the underlying cellular dysfunctions. Classical markers like creatine kinase, lactate dehydrogenase, and myoglobin are indirect but useful in terms of sarcolemmal integrity and muscle fiber stress and complement functional tests (Augusto et al., 2025; Glancy et al., 2021; Hong and Huang, 2025). Nevertheless, none of these biomarkers can be considered a complete reflection of muscle damage since their responses in the bloodstream are affected by inter-individual distances, muscle fibre makeup, training condition, and genetic variations (Sil and Chakraborti, 2025). To this end, biochemical markers are meant to be considered as integrative measures which put in perspective structural and physiological responses instead of predictors of muscle dysfunction.

More current studies have not only expanded the analysis of EIMD injury in terms of classical leakage proteins, but also structural and regulatory proteins, such as skeletal muscle troponins (Bogomolova and Katrukha, 2024), titin fragments (Hansell et al., 2025), and desmin (Agnetti et al., 2022). These indicators provide a better indication of sarcomeric perturbation of the cytoskeleton and remodeling, thus offering mechanistic understanding of myofibrillar integrity in isolation of indirect metabolic leakage (Markus et al., 2021). Although they could assist the development of the specificity of muscle damage assessment, the common usage of these structural biomarkers is not widespread due to the complexity of methods and the unavailability of the standard reference ranges. However, their appearance emphasizes a conceptualization change in molecular-based descriptions of muscle injury and regeneration.

Simultaneously with the biochemical signs of muscle damage, the inflammatory response is one of the primary regulatory aspects of EIMD (Methenitis et al., 2021). Immune signaling cascades triggered by mechanical and metabolic stressors mediate tissue degradation, clearance of debris, and repair. This highly controlled inflammatory response serves a dual purpose of stimulating acute symptomology like muscle soreness with a delayed onset and at the same time triggers mechanisms that are necessary to repair and adapt muscle regeneration (Satija et al., 2025). Notably, balance between pro-inflammatory activation and prompt repair dictates whether inflammation supports or adds to maladaptive processes during muscle damage-repair cascade, which highlights the central importance of inflammation in muscle damage-repair cascade (Wang et al., 2025).

In addition to inflammatory mediators, anabolic and catabolic regulators, such as IGF-1, myostatin, and fibroblast growth factor-2 (FGF-2) and vascular endothelial growth factors (VEGF), are critical in the process of remodelling after exercise (Tabone, 2025). Upregulation of IGF −1 and FGF −2 by exercise stimulates protein synthesis, satellite cell growth, and capillary expansion, and downregulation of myostatin eliminates inhibitory signals on muscle hypertrophy (Qi et al., 2022). Under the control of hypoxia-inducible factor-1 (HIF-1), VEGF supports vascular remodelling and increased oxygen supply, combining metabolic changes with structural stability (Zhu et al., 2023). Together, the coordination of these signaling pathways shows that the damage of muscles is not just an event of breakdown, but a complex adaptive process, which incorporates metabolic, structural and molecular systems.

Although the processes of EIMD are a well-studied topic, the literature available continues to discuss the individual components of the problem in isolation, whether it is ultrastructural changes, biochemical leakage indicators, or inflammatory mediators. Therefore, the interaction of mechanical stress, metabolic perturbations, oxidative signaling and molecular controllers of repair is not fully integrated. In that regard, the current review contributes to the advancement of the field as it can bring together these historically divided views into a single, multi-level pattern that connects structural disruption to biochemical reactions, inflammatory control, and long-term muscle adaptation.

Besides, the paper is the first to relate exercise physiology to molecular biology by providing mechanistic drawings and conceptual models that explain the dynamic operations among mechanical strain, metabolic exhaustion, ROS dynamics, cytokine association and growth -factor signaling. This multi-layered integration moves the existing knowledge a step forward because it frames EIMD as a non-persistent physiological disruption but as a programmed biological process which changes repair, regeneration, and training adaptation.

To operationalize this integrative perspective, the present review follows a systems-oriented framework in which mechanical strain serves as the initiating node, metabolic exhaustion and ROS dynamics act as amplifying mediators, inflammatory signaling functions as a regulatory bridge, and growth-factor pathways determine regenerative versus maladaptive outcomes. This structured cascade is revisited throughout the manuscript to ensure conceptual continuity across structural, biochemical, inflammatory, and molecular domains.

2. Structural and functional organization of skeletal muscle

The skeletal muscle is highly ordered but mechanically susceptible, which makes it prone to damage caused by exercise, especially when exposed to high mechanical loads (Stožer et al., 2020). Myofibrillar and cytoskeletal biomasses are vulnerable to local stress concentration during force transmission across the sarcomere-cytoskeleton-extracellular matrix continuum, making them prone to microstructural disruption in response to the intense or novel exercise (Mavropalias et al., 2023). Muscle fibre composition is another factor that synergizes this vulnerability because the fast-twitch fibres with their large force production and low resistance to fatigue are more sensitive to structural perturbation than slow-twitch fibres (Smith et al., 2023). Taken together, these structural features offer the anatomical foundation on which mechanical overload is converted to the molecular and cellular processes involved in EIMD.

2.1. Mechanisms of EIMD

EIMD is not a response to discrete pathological events but a product of a cascade of tightly linked mechanical, metabolic, and oxidative changes as a result of exercising. Of these, mechanical overload is the stimulus of greatest primary significance especially in the eccentric contractions where the high-force lengthening movements produce a non-uniform strain distribution across the sarcomeres. With this

structural heterogeneity, weaker sarcomeres are prone to over-elongation leading to focal myofibrillar disruption, Z-disk streaming and loss of excitation5contraction coupling (Talebi et al., 2024) (Fig. 1). These mechanically instigated perturbations of the membrane damage membrane integrity and destabilize calcium homeostasis, increasing the threshold to subsequent biochemical and inflammatory reactions (Fig. 2).

Mechanical stress and metabolic fatigue converge to induce sarcomere disruption and calcium dysregulation, initiating downstream inflammatory signaling, proteolytic activation, and delayed-onset muscle soreness (DOMS).

The metabolic fatigue is closely followed by mechanical stress, which increases muscle susceptibility to intense exercise or exercise at the highest intensity (Forman & Mela, 2025). Reduction of adenosine triphosphate, build-up of inorganic phosphate and hydrogen ions, and ionic gradient disruptions all lower force-generating capacity and cause calcium uptake dysfunction. Such metabolic changes do not work in isolation but have a synergistic effect with mechanical strain in terms of worsening calcium dysregulation and triggering proteolytic cascades, which further promotes structural degradation at the myofibrillar level (Tornero-Aguilera et al., 2022; Terrell et al., 2023; Debold and Westerblad, 2024).

Simultaneously, overproduction of reactive oxygen species (ROS) is one of the primary biochemical processes that mediate the connection between mechanical and metabolic stress and downstream tissue damage (Demir et al., 2025a,b). ROS, which result due to mitochondrial respiration, NADPH oxidases, and penetrating immune cells, play a role in lipid peroxidation, protein oxidation, and mitochondrial dysfunction (Özturk et al., 2024). Whereas moderate and low concentrations of ROS play critical roles in muscle adjustment, extreme oxidative stress enhances calcium imbalance and inflammatory processes, thus tipping the scale towards destroying the structure instead of repairing it (Tornero-Aguilera et al., 2022; Tu and Li, 2023).

ROS should not be viewed solely as cytotoxic by-products of metabolism, but rather as redox-sensitive signaling mediators that operate

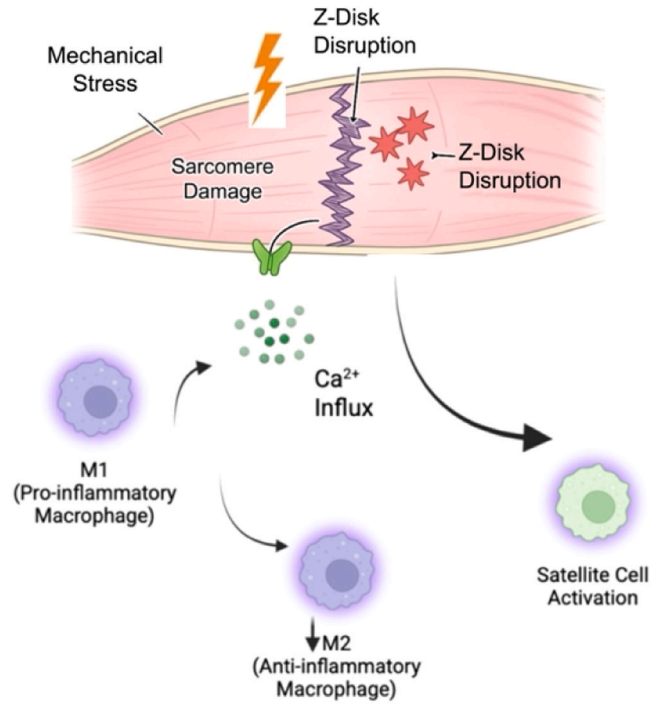

Fig. 1. Mechanical overload induces focal sarcomere disruption and Z-disk streaming, which represent the earliest structural hallmarks of muscle damage. These mechanical irregularities facilitate Ca^{2+} influx through stretch-activated channels, triggering downstream biochemical signaling.

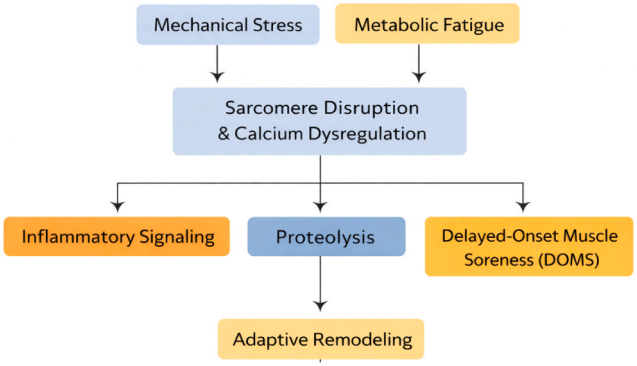

Fig. 2. Integrated mechanistic framework of EIMD.

within a hormetic framework (Nitti et al., 2022). At physiological concentrations, ROS function as second messengers regulating intracellular signaling cascades such as mitogen-activated protein kinases (MAPKs), nuclear factor erythroid 2–related factor 2 (Nrf2), and nuclear factor-κB (NF-κB) (Michalak and Michalak, 2025). Activation of these pathways promotes antioxidant enzyme expression, mitochondrial biogenesis, and cytoprotective adaptations, thereby enhancing skeletal muscle resilience (Pang et al., 2021). In this context, transient ROS elevations following exercise contribute to adaptive remodeling by stimulating redox-sensitive transcription factors and modulating calcium-handling proteins.

Conversely, excessive or prolonged ROS accumulation surpasses endogenous antioxidant capacity, leading to lipid peroxidation, oxidation of contractile proteins, mitochondrial permeability transition pore opening, and amplification of inflammatory signaling (Sikder et al., 2025). High ROS levels further disrupt excitation–contraction coupling by modifying ryanodine receptors and sarcoplasmic reticulum Ca^{2+} ATPase activity, thereby exacerbating calcium dysregulation and proteolytic activation (Michelucci et al., 2021). Thus, ROS exert a dual role in EIMD, acting as adaptive signaling molecules under controlled conditions but becoming pathological mediators when redox homeostasis is disrupted. The balance between ROS production and antioxidant defense capacity ultimately determines whether redox signaling contributes to regeneration or structural degeneration (Wang et al., 2021).

This complex of mechanical, metabolic, and oxidative processes results in the typical functional expressions of EIMD, such as transient loss of force, impaired neuromuscular efficiency and delayed onset muscle soreness (Yasul et al., 2024). Notably, these acute symptoms are not only the symptomatic manifestations of tissue disruption, but also the initiation of coordinated repair and remodelling pathways. EIMD thus should be theoretically viewed as a dynamic spectrum where mechanical overload triggers an avalanche of biochemical and molecular pathways that concomitantly trigger acute dysfunction and skeletal muscle homeostasis in the long-term (Schwiete et al., 2025).

Importantly, these mechanometabolic perturbations do not terminate at the level of structural disruption. Calcium dysregulation and ROS amplification serve as upstream signals that activate inflammatory cascades and subsequently modulate growth-factor expression. Thus, mechanical overload constitutes the initiating trigger of a multi-layered adaptive network rather than an isolated injurious event.

2.2. Acute versus chronic muscle damage: exercise modality and temporal recovery dynamics

Although the previous section has outlined the mechanistic foundation of EIMD, such perturbations vary considerably whether the stimulus is acute or chronic in nature (Stožer et al., 2020). As certification of EIMD in an acute–chronic paradigm is critical to appreciation of how structural disruption translates to adaptation or maladaptation

(Owens et al., 2019). EIMD can be conceptualized according to two biologically separate pathways: sudden disruption after a bout of unaccustomed (Chen and Zhang, 2024) or high-force mechanical loading and repeated microtrauma induced by repetitive exposure to training with incomplete between-sessions recovery (Smith and Gallagher, 2018). Such requirements do not only differ in quantity, but are also temporally organized and regulated.

Acute muscle damage, most frequently associated with eccentric-biased exercise, is characterized by rapid sarcomeric instability, calcium influx, and early ROS amplification (Chalchat et al., 2022). Within the first 24 h, mechanical perturbation dominates. This is followed by a pronounced inflammatory phase (24–72 h), during which neutrophil infiltration and cytokine release peak. The subsequent regenerative phase (3–10 days) involves satellite cell activation and growth-factor–mediated remodeling. When recovery is sufficient, this cascade promotes adaptive hypertrophy and improved stress tolerance (Su and Su, 2025).

In contrast, chronic muscle injury would demonstrate an accumulating effect of repeated loading in the absence of sufficient temporal resolution between inflammatory and redox responses (Smith et al., 2008). Instead of sequential stages, the simultaneous induction of ROS signaling, cytokine production and growth-factor pathways might continue to take place.This sustained perturbation can delay regenerative transitions, blunt adaptive signaling, and potentially predispose the tissue to maladaptive remodeling or overtraining-related dysfunction (Radak et al., 2013; Luti et al., 2020).

The nature of the mode of muscle contraction and the type of mechanical load that is imposed on it have a significant impact on the magnitude and nature of EIMD (Devantier-Thomas et al., 2024). Eccentric contractions are the exercise modalities that always provoke the strongest structural and functional disturbance (Kanzaki et al., 2022), although they may incur similar or even lesser metabolic costs compared to concentric and isometric actions (Ruas et al., 2025) (Fig. 3). The greatest vulnerability to this increase in susceptibility is believed to be the result of high-force lengthening due to non-uniform sarcomere strain, which makes eccentric exercise a very popular experimental model to study EIMD (Qian et al., 2023).

Contrary to that, concentric and isometric contractions tend to cause less muscle damage, since no excessive sarcomere stretch is used to produce force (Kiriaev et al., 2023). Although such modalities can still elicit metabolic stress and a state of transient fatigue, their role in the overall overt structural disruption is relatively minor. Notably, repeated stimulation by harmful exercise, specifically eccentric loading, causes protective mechanisms called repeated bout effect, in which future bouts lead to reduced muscle injury and faster recovery (Rai et al., 2024). Together, these observations emphasize the fact that exercise modality does not only dictate the degree of muscle damage, but also influence the adaptive pathway of skeletal muscle to mechanical stress.

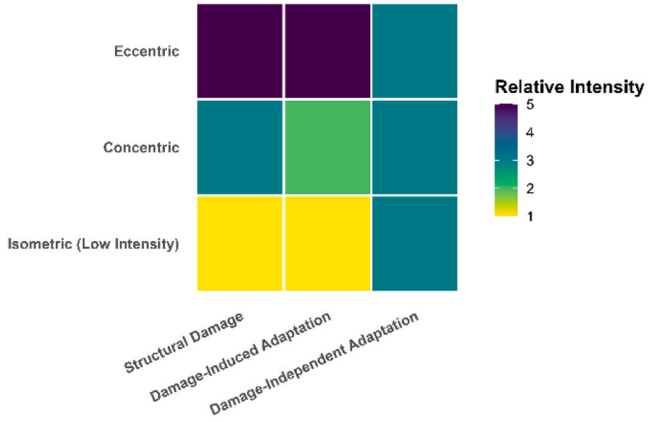

Fig. 3. Differential adaptive pathways across exercise modalities.

Conceptual heatmap illustrating distinct mechanistic routes of skeletal muscle adaptation. Structural damage and damage-induced regenerative adaptation are predominantly associated with eccentric exercise. In contrast, low-intensity isometric exercise induces minimal structural disruption while promoting adaptation primarily through damage-independent metabolic and neuromuscular mechanisms. Color intensity reflects qualitative literature-based estimations rather than quantitative measurements.

Thus, recovery should be understood as the coordinated re-establishment of structural integrity, redox homeostasis, inflammatory resolution, and growth-factor signaling balance. The distinction between acute and chronic damage underscores that muscle injury per se is not inherently detrimental; rather, the timing, magnitude, and integration of these regulatory layers determine whether the outcome is adaptive remodeling or maladaptation.

2.3. Adaptation and recovery following EIMD damage

Despite the fact that short-term effects of EIMD consist of muscle soreness, swelling, and temporary performance declines, the growing body of evidence suggests that EIMD is a source of critical stimuli which makes skeletal muscle adapt to the changes in the long term (Calvo-Rubio et al., 2024). The initial inflammatory and oxidative processes that contribute to the tissue disruption may be utilized when properly controlled as signalling messengers to encourage muscle remodelling, repair, and hypertrophy (Ji et al., 2022). This two-sided nature of damage-related pathways highlights the idea that EIMD is not only a pathological event but a required element of training-induced adaptation.

One of the best-defined examples of this adaptive response is the repeated bout effect according to which previous exposure to eccentric loading provides protection against future muscle damage (Lindsay et al., 2021; Tokuda et al., 2025). This phenomenon indicates structural and functional remodelling of skeletal muscle, such as the degree of strength of the cytoskeleton, neural repositioning, and the optimal distribution of force (Guzman et al., 2025; Zhang et al., 2025). In this connection, the muscle organization, damage processes, and contraction patterns are especially relevant to the etiology of EIMD, but also the dynamic interplay between mechanical loads and reparative processes (Kumar et al., 2025). The acknowledgement of the combined effect of mechanical overload, metabolic fatigue and oxidative signalling as harmful as well as adaptive stimuli is still of central importance in the development of the science of exercise physiology.

2.4. Operational definition and context-dependent criteria for muscle damage

Muscle damage in the context of exercise should not be defined solely by structural disruption or by isolated biochemical markers. Instead, it requires a context-dependent operational framework integrating structural, functional, biochemical, and inflammatory parameters (Brancaccio et al., 2010). Operationally, EIMD may be defined as a transient disturbance in muscle structural integrity and contractile function accompanied by measurable alterations in intracellular enzyme leakage, redox balance, inflammatory signaling, and performance capacity (Powers and Jackson, 2008; Baird et al. 2012; Baumert et al., 2016).

Importantly, Crucially, the direction and explanation of these changes can be modulated by the mode of exercise performed, participants training status and timing. Acute eccentric loading often results in marked structural damage and enzyme elevation, while endurance exercise may lead to substantial metabolic and redox disturbances with only modest sarcomeric injury. Chronic or repeated loading conditions may have a smaller biochemical peak and prolonged inflammation or functional disorders (Stožer et al., 2020). Hence, muscle damage assessment should be based on a composite rather than single marker

profiles. Functional measurements (e.g., force loss), circulating biomarkers (e.g., CK, LDH), inflammatory mediators and imaging-based structural evaluations together create a multidimensional profile of tissue perturbation (Fig. 4).

3. Biochemical markers of muscle damage

Biochemical markers should not be interpreted as isolated laboratory measurements but as circulating reflections of the mechanometabolic-inflammatory cascade described in the preceding section. Their temporal patterns provide indirect insight into the progression from structural disruption to immune activation and eventual regenerative signaling. The diagnosis of EIMD depends not on such functional outcomes as force loss and delayed onset muscle soreness (DOMS) but on biochemical indicators reflecting the structural and cellular disturbances (Chalchat et al., 2022). The most common biomarkers in among them, creatine kinase (CK), lactate dehydrogenase (LDH), myoglobin (Mb), and troponins, can provide a specific understanding of the pathophysiology of muscular injury (Table 1). These markers are emitted into circulation after sarcolemmal or myofibrillar integrity has been disrupted and give indirect but useful measures of the magnitude of muscle damage, time course and kinetics of recovery (Billings et al., 2021; Mu et al., 2025).

It is important to acknowledge that no universally accepted physiological thresholds currently exist to distinguish functional EIMD damage from excessive or maladaptive responses. This limitation reflects the inherently individualized nature of muscle damage kinetics rather than a deficiency of the biomarkers themselves. Consequently, absolute cut-off values appear less informative than relative changes from individual baselines, rate of biomarker elevation, and recovery kinetics across repeated exercise bouts. Such individualized interpretation aligns more closely with the principles of personalized training and load management.

3.1. Creatine kinase (CK)

CK has been considered the most classic biochemical marker of muscle damage. Being a cytosolic enzyme that is the heart of energy buffering through phosphocreatine system, CK is generally compartmentalized in muscle fibers (Lygate et al., 2024). The interaction between CK release and sarcolemmal permeability is well-established when muscle injury occurs due to impairment of sarcolemmal integrity during exercise, CK will leak into the interstitial space, and consequently, be carried to the bloodstream, where its high levels are considered a surrogate endpoint of muscle damage (Owens et al., 2019). During the eccentric contractions, mechanical stress is known to destabilize the lipid bi-layer and cytoskeleton anchoring complexes to allow the escape of the cytosolic proteins. The literature indicates that after eccentric exercise, plasma CK increases gradually but significantly with a high level at 24–96 h after exercise (Fig. 5) and slowly returns to normal in 5–7 days (Radišić Biljak et al., 2025). This time series resembles the initiation and recovery of DOMS, which supports the use of

Table 1
Characteristics of common biomarkers used to assess skeletal muscle damage.

Marker	Primary indication	Temporal response	Key limitation
CK	Sarcolemmal disruption	Delayed (24–96 h)	High variability
LDH	Metabolic leakage	Early–moderate	Low specificity
Myoglobin	Acute muscle stress	Very early	Rapid clearance
Titin fragments	Sarcomeric damage	Delayed	Limited availability
Desmin	Cytoskeletal disruption	Progressive	Methodological complexity

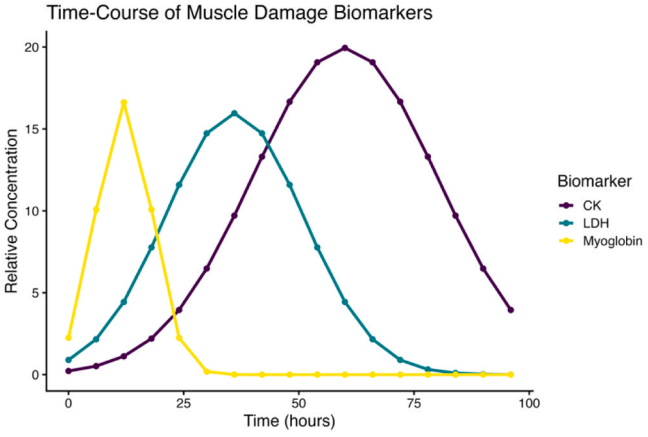

Fig. 5. Temporal profiles of EIMD biomarkers.

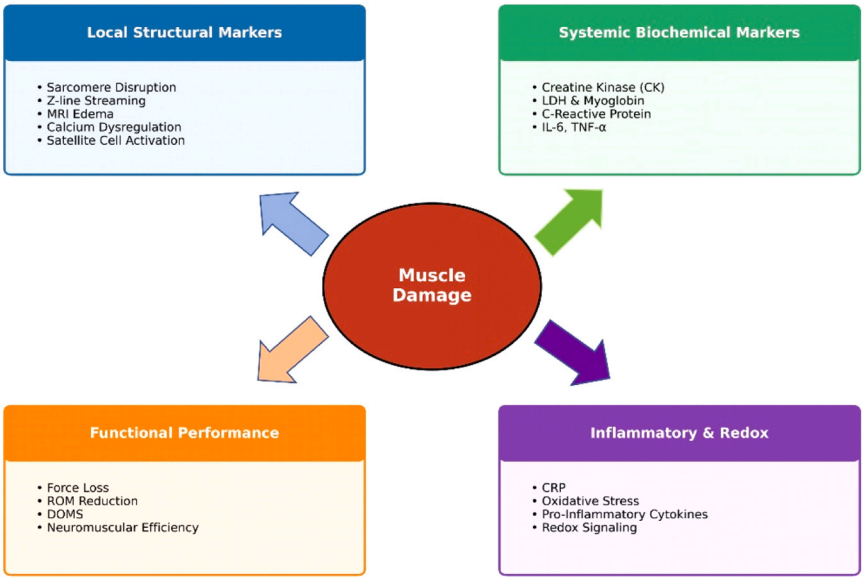

Fig. 4. Context-dependent operational framework for assessing EIMD.

CK as a convenient yet indirect indicator of muscle injury. Nevertheless, CK has a high inter-individual variation. Others are known as high responders, and they exhibit severe elevations (usually >10,000 U/L) in response to analogous exercise stimuli, whereas others exhibit small enhancements in response to analogous structural disruption (Lecina et al., 2024). This variability is caused by genetic factors, muscle fiber composition, and the previous history of training (Cheung et al., 2003). Besides, the release of CK does not necessarily relate linearly with functional impairments like the loss of force, which indicates that CK is a sensitive biomarker of sarcolemmal perturbation, but does not predict performance outcomes (Odriozola et al., 2025). However, CK is also a cornerstone biomarker as it is easy to access, cheap and can be used in research and real-life applications (Sheikh and Kashani, 2025). In sports, CK monitoring is often used to measure recovery status and training load (Haller et al., 2022). In clinical practice, CK is a major diagnostic tool in the conditions of rhabdomyolysis and muscular dystrophies (De Freitas Nakata et al., 2021). The duality of CK as a physiological indicator of transient exercise-induced stress and a pathological indicator of muscle disease is an important issue that highlights its primary role in muscle biology (Xu et al., 2025).

Relative concentrations of CK, LDH, and myoglobin following muscle injury. Myoglobin peaks rapidly within the first 24 h, LDH shows a moderate rise with an earlier decline, while CK demonstrates a delayed and prolonged elevation. These characteristic release patterns reflect different aspects of muscle fiber disruption and metabolic stress.

3.2. Lactate dehydrogenase (LDH)

Another cytosolic enzyme that is commonly used together with CK to measure muscle damage is LDH. Structurally LDH catalyzes the conversion between the pyruvate and lactate in glycolysis and, similar to CK, it is usually localized within the intracellular space (Bartoloni et al., 2024). Destruction of the sarcolemma or the connected membranes permits the escape of LDH into the blood, indicating high activity in the serum that leads to a violation of cell integrity (Washington and Schrems, 2025). LDH has a higher tendency to increase more acutely after exercise as compared to CK, which is usually at its peak after the first 24–48 h (Fig. 5). This response has prompted other researchers to suggest that LDH is a better immediate indicator of cell disruption, but its level of increase is typically lower than CK (Ergenc et al., 2023). Moreover, LDH activity is not so specific on skeletal muscle, since it is also contained in cardiac tissues, hepatic tissues and erythrocytic tissues (Puranik et al., 2021). Exercise-induced gains should therefore be viewed with care, especially when dealing with a mixed population or when dealing with individuals having comorbid ailments. In spite of such limitations, LDH is still useful in defining the level of membrane injury (Wertheimer et al., 2018). Together with CK it gives a more full profile of exercise induced perturbations with CK showing cumulative and delayed disruption and LDH showing acute membrane compromise. Such a dual-marker strategy has been used in many exercise studies in an attempt to triangulate muscle damage response timing and severity (Salem et al., 2024). Notably EIMD, including interventions aimed at reducing it, like the supplementation of branched-chain amino acids, has been found to cause less development of CK and less impact on LDH, thus suggesting that they are regulated differently (Boukhris et al., 2020). These results support the idea that CK and LDH are two different indicators of cell leakage that represent different facets of the muscle injury process.

3.3. Myoglobin (Mb)

Another marker of exercise-induced damage that is well validated is Mb, a hem-containing oxygen-binding protein located in the cytoplasm of skeletal muscle fibres (Zoladz et al., 2024). Mb in contrast, is a very small molecule (around 17 kDa) and can easily be diffused into the circulation due to even small perturbations of membrane integrity unlike CK and LDH (Brancaccio et al., 2010). As a result, the levels of Mb have increased quickly, typically in hours following workouts, so it is an early sign of muscular harm (Nikolaidis et al., 2008). This high-speed kinetic character gives it unique benefits. In contrast to CK which normally peaks days following detrimental exercise, the Mb levels can rise practically instantly, providing instantaneous information on muscle stress (Baird et al., 2012). Mb is especially useful in those settings where acute measure is needed, endurance training, military training, or even in high-intensity interval training. Nevertheless, Mb is also characterized by quick clearance, and the level returns to the baseline in about 24 h, which restricts the application of this medication in long-term monitoring of recovery (Di Battista et al., 2018). One more benefit of Mb is that it has a relative specificity to skeletal and cardiac muscle. Mb has found clinical application in the detection of myocardial infarction in its early phases; however, its diagnostic use has been diminished by troponins because of lack of cardiac specificity and rapid clearance (Asl and Rahimzadegan, 2022). The bifid quality of Mb of both muscle types in exercise physiology is not so problematic because when it rises after skeletal muscle activity, it can easily be put into context. All in all, it is possible to note that Mb is a sensitive, short-term measure of sarcolemmal perturbation. The fact that it is used in conjunction with CK and LDH increases the temporal sensitivity of biochemical surveillance where researchers and practitioners are able to identify the early, acute stage of muscle damage without the longer-lasting biomarkers becoming inflated (Kusmierczyk et al., 2024).

3.4. Troponins and structural protein biomarkers

Troponins are integral components of the thin filament regulatory complex and play a fundamental role in excitation–contraction coupling by modulating actin–myosin interactions in response to calcium signaling (Jeon et al., 2022). In clinical practice, cardiac-specific troponins are widely used as sensitive markers of myocardial injury (Lazar et al., 2022). However, accumulating evidence demonstrates that strenuous or prolonged exercise can induce transient elevations of circulating troponin concentrations in the absence of overt cardiac pathology (Aengevaeren et al., 2021). From an exercise physiology perspective, these exercise-associated troponin responses are increasingly interpreted as reflecting reversible contractile stress and heightened membrane turnover rather than irreversible tissue damage (Khetarpal et al., 2025). Importantly, emerging data suggest that troponin release following intense exercise may originate, at least in part, from skeletal muscle sources or from physiological membrane remodeling processes, emphasizing the need for cautious and context-dependent interpretation (Rasmussen and Jin, 2021).

In skeletal muscle trauma, such a clinical usefulness of troponins goes further than a mere diagnostic equivalent to pathological injury; their appearance can represent subtle changes of myofibrils caused by high mechanical stress (Yamada et al., 2019). Exercise programs with a large proportion of eccentric exercises are specifically skillful in causing the increase in transient troponin levels, which is in line with the idea that such exercises put a heterogeneous sarcomere strain and interfere with the excitation-contraction coupling (Borkowski et al., 2023). However, due to any overlap of skeletal and cardiac troponins, and the increased sensitivity of modern assays, troponin measurements are to be cautiously interpreted along with exercise modality, training status, and other physiological indices (Aakre & Omland, 2019; Rasmussen Jin, 2021).

In addition to troponins, other structural proteins including titin and desmin provide more mechanistically informative information on EIMD (Krüger and Kotteer, 2016). Titin is a giant human protein that extends across about half of the sarcomere and can be said to serve as a molecular spring, which generates passive tension, sarcomere stability, and force transmission (Herzog, 2018). Eccentric training causes significant tension on titin leading to partial unfolding or fragmentation that has been significantly associated with reduced force-generating ability and

slower recovery (Harris-Love et al., 2021). Subsequently, the identification of titin fragments in the circulation or in the urine after harmful exercise has been suggested as a sensitive signal of the sarcomeric disruption thus, offering a period to the conventional leakage markers (Sipos et al., 2025).

An intermediate filament protein called desmin is important in ensuring that myofibrillar orientation and structural integrity of muscle fibers are maintained (Agnetti et al., 2022). Damage due to exercise could lead to desmin degradation probably due to mechanical overload and Ca dependent proteolytic activity a reflection of cytoskeletal release and necessary over- remodeling (Kano et al., 2012). Changes in desmin are further more directly reflective of the integrity of the intracellular scaffold involved in force transmission than cytosolic enzymes thereby making it particularly relevant to recovery kinetics and susceptibility to subsequent damage (Agnetti et al., 2022).

Despite robust mechanistic relations, troponins and other structural protein biomarkers for exercise are restricted by methodological (analytical complexities, cost and lack of standardized reference ranges). Moreover, there is also the consideration of inter-individual differences and assay sensitivity that further confound a cross study comparison. Thus, structural protein biomarkers should not necessarily be viewed as replacements for conventional markers but rather complementary tools that allow muscle damage measurement to be more specific. Using other measures of function, as well as more classical biochemical marks, those same proteins give an increasingly nuanced reflection of the area between membrane perturbation and contractile remodelling (Baker et al., 2019; Stemmerik et al., 2025).

Troponins, titin fragments and desmin, when combined, form a superior-order group of biomarkers that are able to reflect the structural aspect of EIMD. The fact that they feature in research paradigms is indicative of a conceptual shift in the discipline with the emphasis moving away on gross enzymatic leakage and providing more specificity to the definition of myofibrillar and cytoskeletal disruption. This integrative picture is consistent with the new pattern of seeing EIMD as a controlled and adaptive process where structural remodelling can be both an outcome of the mechanical stress and a condition of future functional adaptation.

While functional outcomes such as strength loss, performance decrements, and perceived soreness remain the most direct indicators of exercise-induced impairment, blood biomarkers provide complementary rather than superior information. Their primary contribution lies in contextualizing functional data, particularly in situations where external performance appears preserved despite elevated internal physiological stress. Therefore, biomarkers should be viewed as confirmatory tools that enhance interpretability rather than as independent predictors of functional recovery.

4. Inflammatory responses to muscle damage

A key part of the pathophysiology of EIMD is the inflammatory reaction, which mediates the process of initial mechanical perturbation to the following process of repair and adaptation (Peake et al., 2017). Damage-related molecular patterns extracellularly released by injured fibers in response to structural perturbation of sarcolemma and myofibrillar apparatus trigger innate immune signaling pathways (Mukund and Subramaniam, 2020). The early stage is marked by the high expression of pro-inflammatory cytokines, in the first place interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β and coordinate recruitment of leukocytes, vascular permeability, and phagocytic clearance of cellular debris (Fujiyoshi et al., 2022). These processes form the basis of the classical clinical presentation of EIMD, which is DOMS, temporary decreases in force-generating capacity, and localized edema (Fig. 6).

The diagram illustrates the pleiotropic and interconnected roles of inflammatory and regulatory cytokines in the progression from muscle damage to regeneration. Structural disruption and Ca^{2+} dysregulation

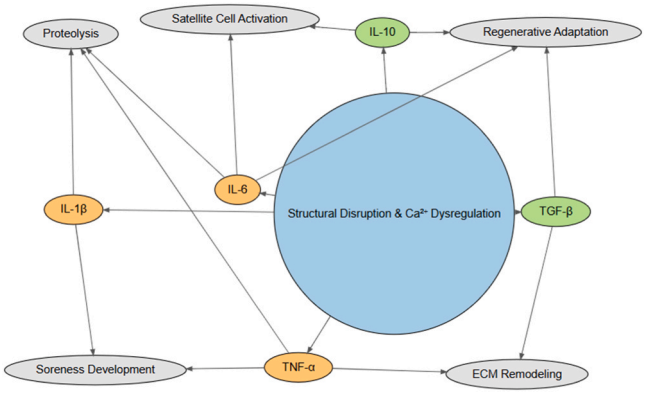

Fig. 6. Integrated cytokine interaction network during muscle regeneration following structural disruption and Ca^{2+} dysregulation.

initiate cytokine signaling cascades involving IL-6, TNF-α, IL-1β, IL-10, and TGF-β.

The role of IL-6 among these mediators is a rather complicated and multidimensional one. IL-6 rapidly leaks out of contracting skeletal muscle fibers, indicative of metabolic stress, e.g., glycogen depletion, and mechanical workload, and eccentric exercise precipitates particularly strong increases (Lin et al., 2023). Although IL-6 is considered as a pro-inflammatory cytokine, its role in exercise goes beyond inflammation, also triggering the hepatic acute-phase response, regulating the mobilization of substrates, and initiating anti-inflammatory signaling pathways (Nash et al. 2023). This duality emphasizes the idea that cytokine responses to EIMD cannot be considered the result of tissue damage but rather the part of a complex physiological reaction to mechanical load (Stožer et al., 2020).

Simultaneously, TNF-α and IL-1β enhance the interaction of inflammation by triggering transcriptional factors like NFkB to induce proteolysis, infiltration of immune cells, and sensitisation of nociceptors (Boakye et al., 2021). Such cytokines play a direct role in causing muscle soreness and premature functional impairment through the amplification of uncoupling of excitation-contraction coupled proteins and catabolism (Sharma and Dabur, 2020) (Fig. 6). However, they are also needed in the acute stage of EIMD to effectively clear of necrotic tissue and trigger downstream regenerative signaling. Therefore, it is not necessarily harmful when the pro-inflammatory cytokines are raised too often or too long, but when they are activated temporarily, it is a required phase in the healing process (Torres-Ruiz et al., 2023).

As the inflammatory response advances, there is a critical transition process towards resolution, which is characterized by a cytokine profile change and immune cell phenotype. Anti-inflammatory cytokines, including interleukin-10 (IL-10) and transforming growth factor-β (TGF-β) gain more powerful influence and suppress excessive pro-inflammatory activity and make the macrophages polarized to regenerative (M2) rather than pro-inflammatory (M1) (Sanjabi et al., 2009; Steen et al., 2020). This process promotes satellite cell activation, extracellular matrix remodelling and myofiber integrity recovery. Notably, the resolution phase does not imply the passive elimination of inflammation but instead an active reprogramming that connects immune signaling to anabolic and regenerative pathways necessary to muscle recovery (Chazaud, 2020).

Physiologically, the temporal regulation of inflammation after EIMD is also largely defining the functional importance of this physiological process. Properly resolved acute inflammatory responses lead to structural reinforcement and adaptive remodeling, which provides a mechanistic basis of the repeated bout effect that is manifested after repeated exposure to eccentric exercise (Margaritelis et al., 2015). Conversely, regeneration can be impaired, delayed (resulting in longer-lasting soreness) and prone to maladaptive effects including overreaching or overtraining syndromes, by chronic or dysregulated inflammation,

which is commonly seen to be caused by overtraining load, undertraining load, or metabolic stress (Magherini et al., 2019). This difference points at the importance of conceptualizing inflammation as a pathology-dependent mediator, the duration and magnitude of which determine the effects of training activities critically.

These implications are of significant significance to exercise prescription and recovery strategies. Over-inhibition of inflammatory cues by the indiscriminate application of anti-inflammatory interventions, including non-steroidal anti-inflammatory drugs or violent cryotherapy may flatten not only soreness but also the molecular stimuli that are necessary to achieve optimal adaptation. By contrast, poor recovery management can allow inflammatory reactions to remain active longer than adaptive, hence reducing muscle quality and performance over time. To this end, the response to muscle damage after exercise must be conceptualized as a highly controlled biological mechanism that combines mechanical stress and molecular repair processes, and eventually defines the threshold between functional recovery and skeletal muscle adaptation.

The resolution phase of inflammation represents a critical transition point in the EIMD continuum. Anti-inflammatory cytokines do not merely suppress tissue damage but actively prime growth-factor signaling pathways, thereby linking immune regulation to anabolic remodeling. This transition marks the shift from damage containment to regenerative adaptation.

5. Growth factors and molecular regulators of muscle repair and adaptation

Growth factors should be conceptualized as downstream integrators of mechanical strain, metabolic stress, ROS dynamics, and inflammatory resolution. Their activation is neither temporally nor mechanistically independent but represents the convergent output of upstream perturbations described in previous sections. Post exercise muscle injury inflammation is resolved by the activation of an integrated web of growth factors and molecular regulators that controls skeletal muscle repair, remodelling and long-term adaptation. These are signaling pathways that show a vital shift of catabolic to anabolic muscle tissue restoration and reinforcement (Egan and Sharples, 2023). Instead of working alone, growth factors act as downstream integrators of mechanical loading, metabolic perturbations, and immune-mediated signaling, which implement temporary structural disruption into permanent physiological adjustment (Long et al., 2025). The insulin-like growth factor-I (IGF-I), myostatin, fibroblast growth factor-2 (FGF-2), and vascular endothelial growth factor (VEGF) are among the most significant regulators in this process and have a role in different but equally connected aspects of myogenesis, angiogenesis, and metabolic support (Luo et al., 2024).

IGF-1 also has a key role in the coordination of skeletal muscle regeneration and hypertrophic response to injury. IGF-1, by acting via systemic endocrine and locally produced autocrine/paracrine isoforms, induces protein synthesis, satellite cell activation, and differentiation, and eventually restores myofiber structure and contractile properties (Bailes and Soloviev, 2021). Mechanical loading, especially resistance and eccentric training, causes muscle-specific isoforms of IGF-1, including mechano-growth factor, strongly linked to the restoration of disrupted sarcomeres and strengthening the cytoskeleton (Sundari and Ar, 2022). Other benefits of long-term exercise-induced increases in IGF-1 include long-term muscle mass and function maintenance, preventing age-related losses, and promoting metabolic fitness (He et al., 2023). In this way, IGF-1 signaling offers a direct molecular connection between mechanical stress and anabolic remodeling, which converts physical stress into adaption responses of cells (Chu et al., 2025). In addition to well-established mediators such as IGF-1 and FGF-2, recent evidence highlights the regulatory role of growth differentiation factor 3 (GDF3) in skeletal muscle regeneration. GDF3 is an anti-inflammatory TGF-β family cytokine that appears to link inflammation, adipose tissue function, and metabolic regulation processes (Wang et al., 2020). Exercise training lowers inflammatory cytokines and improves adipose tissue microenvironment and macrophage polarization, processes mechanistically linked to reduced inflammasome activity (Nyawo et al., 2021) (Fig. 7).

Exercise functions as the primary physiological stimulus that induces the expression and modulation of multiple growth factors involved in skeletal muscle remodeling. Classical mediators such as IGF-1 and FGF-2 contribute to hypertrophic and angiogenic responses, while VEGF promotes angiogenesis and satellite cell activation. In addition to these well-established factors, GDF3, a recently described regulator within the TGF-β superfamily, is incorporated as a novel modulator of regenerative signaling. Myostatin acts as a negative regulator of muscle growth, counterbalancing hypertrophic signaling pathways. The directional arrows represent exercise-driven signaling cascades leading to structural and functional adaptations rather than reciprocal induction of exercise by growth factors.

However, unlike IGF-1 that poses anabolic effects, myostatin is a potent negative regulator of muscle growth that limits excessive hypertrophy by inhibiting the proliferation and differentiation of myoblasts (Chen et al., 2021). High myostatin levels are usually linked to muscle atrophy, poor regenerative response, and low sensitivity to training stimuli (Rodriguez et al., 2014). It has always been demonstrated that exercise inhibits myostatin signaling, thus breaking the inhibitory effects of muscle growth and promoting hypertrophic and regenerative mechanisms (Baig et al., 2022). This mutual regulation of the IGF-1 and myostatin thus forms a key axis that regulates muscle plasticity. Notably, the homeostasis of these contradictory messages dictates the successive response of molecular environment of EIMD to either effective adaption or maladaptive remodelling, which underscores the idea that muscle recovery depends on dynamic regulation interactions rather than discrete molecular events (Yoshida and Delafontaine, 2020).

In addition to myogenesis, myocellular tissue damage can only be compensated successfully through the interactions between vascular and extracellular matrix remodeling. In this respect, FGF 2 is a central figure that leads to fibroblasts activity, extracellular matrix renewal, and angiogenesis (Brenner et al., 2019). Increases in FGF-2 expression in response to exercise have been linked with capillary formation, structural support of myofibers, less fibrotic remodeling, which help maintain muscle elasticity and transmit forces efficiently (Soori et al., 2022). This has been especially noted with repeated mechanical loading, in which a surplus deposition of extracellular matrix can reduce contractile activity

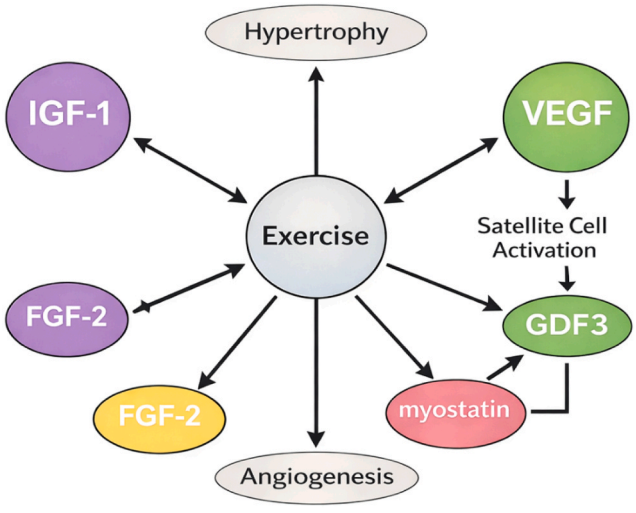

Fig. 7. Exercise-induced growth factor network regulating skeletal muscle adaptation.

and make it susceptible to injury. By acting together with different components of the connective tissue and vascular, FGF-2 is involved in the formation of an appropriate microenvironment that supports repair and adaptation (Ma et al., 2025) (Fig. 7).

VEGF is a major mediator of exercise-induced angiogenesis, which allows the proliferation and remodelling of the capillary network in skeletal muscle (Aragón-Vela and Casuso, 2025). Under the control of hypoxia-inducible factor-1 signalling under conditions of high metabolic activity, VEGF facilitates the proliferation of endothelial cells and the growth of capillary density, which improves oxygen and nutrient delivery to active and recovering muscle fibres (Primer et al., 2020). Such vascular responses not only facilitate tissue repair but also enhance metabolic efficiency and fatigue tolerance during subsequent bouts of exercise. Although VEGF has been widely considered in cardiovascular and neurovascular applications, it is also important in skeletal muscle adaptation because proper vascularization is the basis of the regenerative capacity and long-term performance improvement (Zarezadehmehrizi et al., 2021; Ercan et al., 2023).

Notably, IGF-1, myostatin, FGF-2 and VEGF activities are not chronologically independent but rather coincide in the course of the restoration and constitute an overall regulatory system by coordinating structural, metabolic and vascular modulation (Fig. 7). These pathways should be activated appropriately after EIMD with the aim of increasing muscle resilience and also leading to other protective mechanisms such as the repeated bout effect in which exposure to damaging exercise subsidizes consequent injury. On the other hand, anabolic and angiogenic signalling dysregulation due to excessive load, insufficient rest or chronic inflammation can lead to impaired regeneration, maladaptive extracellular remodelling and chronic dysfunction of muscle tissue predisposition.

From both physiological and practical perspectives, these observations suggest that growth factors function not merely as indicators of tissue repair but as direct mediators of training adaptations. The magnitude and duration of growth factor responses may determine whether EIMD serves as a stimulus for adaptation or progresses toward maladaptation. In line with this, the conceptualisation of growth factors is to include critical molecular mediators which combine inflammatory resolution with mechanical loading and metabolic need, eventually determining which side of the functional recovery to the long-term skeletal muscle adaptation.

5.1. Satellite cells and myogenic regeneration

The adult human body consists of approximately 600 muscles which form the largest body tissue, about 40–50 % of body weight. Skeletal muscle mononuclear stem cells, called satellite cells (SCs). Since then, there is tremendous interest to investigate their application in muscle regeneration and repair due to their special self-renewal and multi-differentiation capabilities (Morgan and Zammit, 2010). Their name pertains to their location, residing between the skeletal myofiber's basal lamina and the plasma membrane. SCs play an important role in after-birth growth and regeneration of skeletal muscle (Forcina et al., 2019). SCs are mitotically quiescent and their state is altered in response to a variety of physiologic and pathologic stimuli such as denervation (Wozniak et al., 2005) and exercise (Neuhaus et al., 2003).

SCs constitute the principal stem cell population responsible for skeletal muscle regeneration following exercise-induced structural disruption (Galimov et al., 2016). Located between the basal lamina and the sarcolemma, these quiescent progenitor cells become activated in response to mechanical strain, calcium dysregulation, inflammatory signaling, and growth factor stimulation. Upon activation, SCs proliferate, differentiate into myoblasts, and subsequently fuse either with existing myofibers to repair damaged regions or with each other to form new myofibers (Snijders et al., 2009).

Pro-inflammatory cytokines released during the early inflammatory phase promote satellite cell proliferation, whereas the transition toward anti-inflammatory signaling supports differentiation and fusion (Perandini et al., 2018). Growth factors such as IGF-1 and FGF-2 enhance myogenic progression, while myostatin acts as a negative regulator limiting excessive proliferation (Ahmad et al., 2023). Emerging evidence also suggests that redox-sensitive pathways, particularly Nrf2-mediated antioxidant signaling, modulate the balance between satellite cell self-renewal and differentiation (Wang et al., 2013). Thus, SCs represent the biological bridge linking inflammatory resolution and growth-factor signaling to structural regeneration. Their activity determines whether EIMD progresses toward effective myofiber repair and hypertrophy or remains in a prolonged state of incomplete regeneration. Within the systems-oriented cascade proposed in this review, satellite cell dynamics function as the central executor of the regenerative phase.

6. Practical implications in sports and rehabilitation

This section translates mechanistic insights into applied decision-making contexts. Such a comprehension of the mechanistic nature of EIMD has both direct and practical implications on athletic training and clinical rehabilitation. Muscle damage should be treated as a strategic component of opportunity to reduce the unreasonable progression of functional deterioration without excessive loss of molecular stimuli that are required in the process of the process of adaptation and repair. Based on this, rational interventions ought to be directed at maximising mechanical loading, restorative approaches and nutritional assistances.

From an applied perspective, blood biomarkers of muscle damage should not be interpreted as standalone indicators guiding training or recovery decisions. Rather, their practical value emerges when they are used as contextual modifiers within an integrated monitoring framework. In elite and sub-elite athletes, biomarkers such as creatine kinase, lactate dehydrogenase, and myoglobin are most informative when assessed longitudinally within the same individual, interpreted relative to personal baseline values, and combined with functional performance measures and subjective recovery indices. Under these conditions, biomarker monitoring can support early identification of excessive internal load accumulation before overt performance decrements become evident.

In practical terms, biomarker assessment is most likely to alter training or recovery decisions in specific scenarios rather than during routine training periods. These include congested competition schedules with limited recovery time, return-to-training or return-to-play phases following injury or prolonged detraining, and cases of suspected non-functional overreaching where performance metrics remain temporarily preserved. In such contexts, elevated or delayed biomarker responses may prompt adjustments in training volume, recovery duration, or exercise modality, thereby reducing the risk of maladaptive outcomes.

6.1. Nutritional strategies to support muscle repair and recovery

Nutritional interventions are complementary and modulative factors with regard to determining the magnitude and temporal profile of EIMD. Proper dietary protein supplement intake is one of the main pillars of post exercise recovery as it has a direct effect of supporting muscle protein synthesis, activation of satellite cells and structural remodelling of the damaged myofibres. The growing body of research reveals that it is not only the total protein intake, but also the timing and the distribution of high-quality protein sources throughout the day and especially during the early post-exercise period that is important in maximising anabolic signalling and counteracting net protein breakdown.

Whey protein (WP) is a highly effective nutritional approach to alleviate muscle damage caused by exercise as pointed out by recent mechanistic research by Li et al. (2025). Their results show that the supplementation of WP is resistant to oxidative-stress-related injury and at the same time, increases skeletal-muscle protein synthesis. On the

molecular level, WP was demonstrated to stimulate the SIRT1/Nrf2/ HO −1 signalling axis, which enhances the natural antioxidant resources and minimizes the overload of ROS. Parallel to this, WP stimulated the AMPK/TSC2/mTOR/4EBP1 pathway, which was successfully deactivated in protein synthesis caused by overloading. These molecular adaptations were then converted into practical physiological gains such as a better muscle morphology, greater body weight due to muscle accretion and physiological performance measures such as grip strength and gait performance of exercise-injured experimental animals. Together these results highlight the dual antioxidant and anabolic effects of WP against muscle repair.

In addition to protein-based interventions, plant-based antioxidant-rich foods also attracted the interest of their possible effects in moderating post-exercise inflammation and oxidative stress. Sinaga et al. (2021) examined the influence of beetroot juice (Beta vulgaris L.) supplementation in submaximal exercise and stated that the levels of circulating C-reactive protein (CRP), which is a sensitive biomarker of exercise-induced inflammation, were reduced significantly after consuming 300 ml of beetroot juice daily. These protective activities were mainly accredited to the high concentration of betalain pigments, which was accompanied by other supporting flavonoid and phenolic acids, which in combination, scavange the free radicals and inhibit the oxidative damage. These results endorse the use of naturally abundant foodstuffs that contain antioxidants as component of an integrative dietary intervention based on recovery.

One polyphenolic compound, Curcumin, derived by Curcuma longa, has also been thoroughly developed in terms of its anti-inflammatory and analgesic effects in the setting of muscle damage. Nicol et al. (2015) showed that curcumin 2.5 g administered 48 h pre and 72 h post eccentric exercise had significant effects on subjective muscle soreness and did not exhibit any negative effects on jump performance. Complementary evidence of Nakhostin-Roohi et al. (2016) indicated that a single dose of 150 mg after exercise was effective to reduce muscle pain at 48–72 h after exercise. In addition, McFarlin et al. (2016) found that an approximate dose of 400 mg per day was the best dose of enough to reduce exercise-induced increases in pro-inflammatory cytokines like TNF-a and IL-8. Collectively, these studies indicate that curcumin supplementation could help with symptom control and inflammatory balance in case it is administered within the right dose range. Hambright et al. (2023) treated progeroid Zmpste24 -/- mice with fisetin once per week over a four weeks period and they found significant improvements in bone microarchitectural integrity. Structural advantages were also coupled with massive down-regulation of senescence and inflammation-related markers, including p16, IL-6 and TGF-β.

Ramirez-Sanchez et al. (2024) have shown that epicatechin is an epimer of cocoa flavonol that has protective effect against muscle atrophy in older age. Epicatechin (1 mg/kg/day-weeks) orally administered over eight weeks in old Sprague-Dawley rats showed a significant increase in muscle strength, endurance, and mass, which were linked to an improved level of IGF-1, Akt/mTORC1 anabolic pathway, and inhibition of the pro-inflammatory cytokine TNF-α and NF-kB signature.

An accumulating body of evidence supports the use of a food-first solution to the intake of antioxidants. It seems to be safer and more compatible with long-term adaptations than high-dose supplementation when the vitamins C, E, and A are obtained in a balanced and diverse diet and are known to significantly suppress the positive exercise-induced signalling responses (Vo et al., 2023). Vitamin E has been used long as an experimental model of antioxidant in skeletal-muscle injury because it has the ability to normalize intracellular redox flux and protect membrane integrity. A recent meta-analysis study by Kim et al. (2022) came to the conclusion that the use of vitamin E supplement is a successful scavenger of free radicals and inhibiting the release of inflammatory mediators in EIMD models. However, even though these are positive acute effects, one should take precautions with the case of chronic high-dose antioxidant supplementation. According to an emerging literature consensus, too much antioxidant supplementation, especially in isolated form, can cause the loss of redox-sensitive signalling pathways that are critical in the adaptation process to training.

Besides proteins and antioxidants, lipid-based and microbiota targeted nutritional interventions have also become possible modifiers of muscle restoration. It has been demonstrated that omega-3 polyunsaturated fatty acids (n −3 FA), which are most frequently obtained through fish oil, can stimulate anti-inflammatory signalling pathways and can inhibit muscle loss during intervals of disuse by promoting anabolic sensitivity and subsequently protein synthesis. There is growing evidence that suggests that n-3 PUFA supplementation has numerous positive effects in athletes, such as preventing exercise-related fatigue, inhibiting the synthesis of pro-inflammatory cytokines, reducing the synthesis of eicosanoids, and enhancing muscle mass, strength, recovery efficiency, and training adaptation (Tsuchiya et al., 2016; Tinsley et al., 2017; Black et al., 2018).

6.2. *Cold exposure, compression, and active recovery*

Recent years have seen the emergence of a number of interventions aimed at accelerating recovery, including cold water immersion (Moore et al., 2023), contrast bathing (Horgan et al., 2023), and compression garments (CG) (Hill et al., 2014). Research examining the effects of ice-based interventions on exercise-induced inflammation and muscle soreness has produced inconsistent findings. Howatson and Van Someren (2003) reported that ice massage reduced creatine kinase levels, a marker of muscle damage, but did not exert significant effects on other recovery-related outcomes. These observations were supported by subsequent work showing that ice massage failed to attenuate indirect markers of muscle damage or improve muscle function (Howatson et al., 2005). In contrast, cold-water immersion has been associated with a more rapid recovery of counter movement jump performance, accompanied by a normalization and stabilization of creatine kinase levels. These findings suggest that cold-water immersion may preferentially facilitate recovery of stretch–shortening cycle performance, with evidence indicating that moderately warmer water temperatures could be more effective for recovery following strenuous exercise (Vieira et al., 2016).

In a clinical setting, CG have been shown to compress dilated veins and reduce venous reflux to enhance venous return and reduce oedema. This also increases “muscle pump’’ to accelerate blood flow (O'Riordan et al., 2023). A similar mechanism may underlie the benefits of CG in an exercise setting. For example, enhanced recovery of strength and power performance is frequently reported alongside reduced levels of oedema (Kraemer et al., 2001). While the successful management of oedema helps to reduce DOMS and increase mobility, this effect may also attenuate the progression of muscle damage. Fluid accumulation in muscle tissue increases osmotic pressure and subsequent cell lysis, while CG have been shown to reduce cellular trauma alongside swelling (Valle et al., 2014). Reductions in circulating levels of the intramuscular protein CK are frequently reported when CG are worn following exercise (Davies et al., 2009). Haemodynamic effects of CG have also been postulated to aid recovery by enhancing levels of nutrient delivery and metabolite removal (Born et al., 2013). Accordingly, observations of reduced muscle damage following post-exercise compression have been suggested to reflect enhanced cellular regeneration and protein synthesis made possible by enhanced circulation.

7. Conclusion

EIMD should not be interpreted as a collection of isolated structural, biochemical, or inflammatory events. Rather, it represents a dynamic and interconnected biological continuum in which mechanical strain initiates sarcomeric disruption, metabolic exhaustion amplifies redox imbalance, and calcium dysregulation facilitates inflammatory activation. These upstream perturbations converge on cytokine-mediated regulation and growth-factor signaling pathways that ultimately

determine whether tissue injury culminates in adaptive remodeling or maladaptive degeneration. Within this systems-oriented framework, reactive oxygen species function not merely as by-products of metabolic stress but as signaling intermediates linking mechanical load to immune modulation. Inflammatory mediators, in turn, act as transitional regulators that coordinate debris clearance while simultaneously priming anabolic pathways. Growth factors such as IGF-1, FGF-2, VEGF, and emerging regulators including GDF3 integrate these upstream signals to consolidate hypertrophic, angiogenic, and neuroprotective adaptations. Thus, the outcome of EIMD depends less on the presence of damage itself and more on the magnitude, timing, and coordination of these overlapping regulatory layers.

By synthesizing structural, biochemical, inflammatory, and molecular dimensions within a unified mechanistic cascade, this review advances a systems-level perspective of muscle injury and adaptation. This integrative model reframes EIMD not as a pathological endpoint but as a biologically orchestrated process in which controlled perturbation serves as the foundation for long-term functional improvement. Future research should therefore focus on the temporal synchronization and cross-talk among these pathways to better distinguish adaptive from maladaptive trajectories in response to exercise.

8. Future directions

Although there has been a significant development in the understanding of the mechanisms of muscle damage that occur with exercise, there are still some important gaps that the future studies should focus on. In the first place, there is an urgent necessity to develop and validate integrated biomarker panels consisting of classical leakage enzymes along with the structural and molecular biomarkers. These multimetric methods would enhance specificity, minimize inter-individual variation, and increase the temporal discrimination of muscle traumatic detection between various exercise modalities and groups. Second, future research must focus on longitudinal and systems-level research studies that can connect acute molecular reactions with long-term changes. However, most existing studies have described the independent pathways; there is still a lack of understanding of the dynamic interactions between mechanical loading, redox signaling, inflammatory response as well as growth factor activation during repeated training sessions. The new ways to understand the individualized progress of muscle damage and recovery can be provided by advanced omics-based methods in combination with high-resolution imaging and machine-learning-based modeling.

Third, more focus should be put on population-specific reactions to EIMD. The inflammatory, anabolic, and regenerative capacities between aging individuals, clinical populations, and elite athletes differ significantly but most of the literature is based on the younger and healthier cohorts. Individualized research studies are thus needed to narrow down the exercise prescription, nutritional, and recovery interventions under varying physiological and pathological conditions. Lastly, the long-term effects of the popular recovery modalities cryotherapy, antioxidant supplementation and compression strategies need to be reconsidered. Future studies ought to extend past the short-term alleviation of symptoms to determine the effects of repetitive application of such interventions on the molecular signaling, muscle plasticity, and training adaptation in long-term. Elucidating these trade-offs would be fundamental to the translation of mechanistic knowledge to the evidence-based practice.

To sum up, transformative, longitudinal, and personalized studies that go beyond the reductionist paradigms will be needed to develop the area of EIMD further. With increased appreciation of the complexity of skeletal muscle biology, future research can make a better effort to utilize muscle damage as a controllable adaptation stimulus instead of a performance- and health-limiting factor.

CRediT authorship contribution statement

Kübra Özdemir: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Yeliz Demir:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation.

Declaration of Generative AI and AI-assisted technologies in the writing process

Our research team utilized AI-assisted tools solely for language enhancement and readability improvement during the manuscript preparation process.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

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References

Aakre, K.M., Omland, T., 2019. Physical activity, exercise and cardiac troponins: clinical implications. Prog. Cardiovasc. Dis. 62 (2), 108–115.
Aengevaeren, V.L., Baggish, A.L., Chung, E.H., George, K., Kleiven, Ø., Mingels, A.M.A., Ørn, S., Shave, R.E., Thompson, P.D., Eijsvogels, T.M.H., 2021. Exercise-induced cardiac troponin elevations: from underlying mechanisms to clinical relevance. Circulation 144 (24), 1955–1972.
Agnetti, G., Herrmann, H., Cohen, S., 2022. New roles for desmin in the maintenance of muscle homeostasis. FEBS J. 289 (10), 2755–2770.
Ahmad, S.S., Chun, H.J., Ahmad, K., Shaikh, S., Lim, J.H., Ali, S., Han, S.S., Hur, S.J., Sohn, J.H., Lee, E.J., Choi, I., 2023. The roles of growth factors and hormones in the regulation of muscle satellite cells for cultured meat production. J. Anim. Sci. Technol. 65 (1), 16–31.
Aragón-Vela, J., Casuso, R.A., 2025. Effect of hypoxia-inducible factor 1 on vascular endothelial growth factor expression in exercised human skeletal muscle: a systematic review and meta-analysis. Am. J. Physiol. Cell Physiol. 329 (1), C272–C282.
Asl, S.K., Rahimzadegan, M., 2022. The recent progress in the early diagnosis of acute myocardial infarction based on myoglobin biomarker: nano-aptasensors approaches. J. Pharm. Biomed. Anal. 211, 114624.
Augusto, R.S., Dill, A., Souza, E., Nogueira, T.L.S., Gomes, D.V., Paiva, J., Dornelas-Ribeiro, M., Santos, C.G.M., 2025. Kinetics of serum myoglobin and creatine kinase related to exercise-induced muscle damage and ACTN3 polymorphism in military paratroopers under intense exercise. J. Funct. Morphol. Kinesiol. 10 (4), 381.
Baig, M.H., Ahmad, K., Moon, J.S., Park, S.Y., Ho Lim, J., Chun, H.J., Qadri, A.F., Hwang, Y.C., Jan, A.T., Ahmad, S.S., Ali, S., Shaikh, S., Lee, E.J., Choi, I., 2022. Myostatin and its regulation: a comprehensive review of myostatin inhibiting strategies. Front. Physiol. 13, 876078.
Bailes, J., Soloviev, M., 2021. Insulin-like growth factor-1 (IGF-1) and its monitoring in medical diagnostic and in sports. Biomolecules 11 (2), 217.
Baird, M.F., Graham, S.M., Baker, J.S., Bickerstaff, G.F., 2012. Creatine-kinase-and exercise-related muscle damage implications for muscle performance and recovery. J. Nutr. Metab. 2012 (1), 960363.
Baker, P., Leckie, T., Harrington, D., Richardson, A., 2019. Exercise-induced cardiac troponin elevation: an update on the evidence, mechanism and implications. IJC Heart Vasc. 22, 181–186.
Bartoloni, B., Mannelli, M., Gamberi, T., Fiaschi, T., 2024. The multiple roles of lactate in the skeletal muscle. Cells 13 (14), 1177.
Baumert, P., Lake, M.J., Stewart, C.E., Drust, B., Erskine, R.M., 2016. Genetic variation and exercise-induced muscle damage: implications for athletic performance, injury and ageing. Eur. J. Appl. Physiol. 116 (9), 1595–1625.
Billings, A., Quinn, J.K., Spoor, M.S., 2021. Laboratory markers of muscle injury. Equine Hematol. Cytol. Clin. Chem. 119–141.
Black, K.E., Witard, O.C., Baker, D., Healey, P., Lewis, V., Tavares, F., Christensen, S., Pease, T., Smith, B., 2018. Adding omega-3 fatty acids to a protein-based supplement during pre-season training results in reduced muscle soreness and the better maintenance of explosive power in professional Rugby Union players. Eur. J. Sport Sci. 18 (10), 1357–1367.

Boakye, P.A., Tang, S.J., Smith, P.A., 2021. Mediators of neuropathic pain; focus on spinal microglia, CSF-1, BDNF, CCL21, TNF-α, Wnt ligands, and interleukin 1β. Front. Pain. Res. 2, 698157.
Bogomolova, A.P., Katrukha, I.A., 2024. Troponins and skeletal muscle pathologies. Biochemistry (Moscow) 89 (12), 2083–2106.
Bolger, C., Mara, J., Pyne, D.B., McKune, A.J., 2025. Beyond the hit: muscle and vascular tissue responses to contact exposure in collision sports—a narrative review. Sports Med. 55 (11), 2753–2771.
Borkowski, J., Stefaniak, T., Cych, P., 2023. Changes in skeletal muscle Troponin T and Vitamin D Binding Protein (DBP) concentrations in the blood of male amateur athletes participating in a marathon and 100 km adventure race. Int. J. Environ. Res. Public Health 20 (9), 5692.
Born, D.P., Sperlich, B., Holmberg, H.C., 2013. Bringing light into the dark: effects of compression clothing on performance and recovery. Int. J. Sports Physiol. Perform. 8 (1), 4–18.
Boukhris, O., Trabelsi, K., Abdessalem, R., Hsouna, H., Ammar, A., Glenn, J.M., Bott, N., Irandoust, K., Taheri, M., Turki, M., Ayadi, F., Bragazzi, N.L., Engel, F.A., Chtourou, H., 2020. Effects of the 5-m shuttle run test on markers of muscle damage, inflammation, and fatigue in healthy male athletes. Int. J. Environ. Res. Public Health 17 (12), 4375.
Brancaccio, P., Lippi, G., Maffulli, N., 2010. Biochemical markers of muscular damage. Clin. Chem. Lab. Med. 48 (6), 757–767.
Brenner, D.R., Ruan, Y., Adams, S.C., Courneya, K.S., Friedenreich, C.M., 2019. The impact of exercise on growth factors (VEGF and FGF2): results from a 12-month randomized intervention trial. Eur. Rev. Aging Phys. Act. 16 (1), 8.
Calvo-Rubio, M., Garcia-Dominguez, E., Tamayo-Torres, E., Soto-Rodríguez, S., Olaso-Gonzalez, G., Ferrucci, L., Gómez-Cabrera, M.C., 2024. The repeated bout effect evokes the training-induced skeletal muscle cellular memory. Free Radic. Biol. Med. 225, 247–254.
Chalchat, E., Gaston, A.F., Charlot, K., Peñailillo, L., Valdés, O., Tardo-Dino, P.E., Nosaka, K., Martin, V., Garcia-Vicencio, S., Siracusa, J., 2022. Appropriateness of indirect markers of muscle damage following lower limbs eccentric-biased exercises: a systematic review with meta-analysis. PloS One 17 (7), e0271233.
Chatzinikita, E., Maridaki, M., Philippou, A., 2025. Mechanotransduction in Skeletal Muscle. In Fundamentals of Recovery, Regeneration, and Adaptation to Exercise Stress: An Integrated Approach. Springer Nature Switzerland, Cham, pp. 163–184.
Chazaud, B., 2020. Inflammation and skeletal muscle regeneration: leave it to the macrophages! Trends Immunol. 41 (6), 481–492.
Chen, S., Zhang, C., 2024. Effects of ischaemic post-conditioning on eccentric exercise-induced muscle damage. Biol. Sport 41 (2), 27–35.
Chen, M.M., Zhao, Y.P., Zhao, Y., Deng, S.L., Yu, K., 2021. Regulation of myostatin on the growth and development of skeletal muscle. Front. Cell Dev. Biol. 9, 785712.
Cheung, K., Hume, P., Maxwell, L., 2003. Delayed onset muscle soreness: treatment strategies and performance factors. Sports Med. 33 (2), 145–164.
Chu, R., Li, M., Xie, Y., Du, Y., Ni, T., 2025. Exercise interventions and serum IGF-1 levels in older adults with frailty and/or sarcopenia: a systematic review and meta analysis. Front. Public Health 13, 1660694.
Davies, V., Thompson, K.G., Cooper, S.M., 2009. The effects of compression garments on recovery. J. Strength Cond. Res. 23 (6), 1786–1794.
De Freitas Nakata, K.C., da Silva Pereira, P.P., Riveros, B.S., 2021. Creatine kinase test diagnostic accuracy in neonatal screening for Duchenne Muscular Dystrophy: a systematic review. Clin. Biochem. 98, 1–9.
Debold, E.P., Westerblad, H., 2024. New insights into the cellular and molecular mechanisms of skeletal muscle fatigue: the Marion J. Siegman Award Lectureships. Am. J. Physiol. Cell Physiol. 327 (4), C946–C958.
Demir, Y., Ceylan, H., Karağaç, M.S., Türkeş, C., Karaman, M., Beydemir, Ş., 2025a. Esculetin attenuates doxorubicin-induced cardiotoxicity via modulation of apoptotic and mitochondrial gene expression networks. Cell Biol. Int. 49 (12), 1705–1715.
Demir, Y., Ceylan, H., Yeşilkent, E.N., Kizir, D., Karaman, M., Türkeş, C., Beydemir, Ş., 2025b. Esculetin attenuates doxorubicin-induced cardiac toxicity: Evidence from gene expression, enzyme activity, and molecular docking analyses. Comput. Biol. Chem., 108654
Devantier-Thomas, B., Deakin, G.B., Crowther, F., Schumann, M., Doma, K., 2024. The impact of exercise-induced muscle damage on various cycling performance metrics: a systematic review and meta-analysis. J. Strength Cond. Res. 38 (8), 1509–1525.
Di Battista, A.P., Moes, K.A., Shiu, M.Y., Hutchison, M.G., Churchill, N., Thomas, S.G., Rhind, S.G., 2018. High-intensity interval training is associated with alterations in blood biomarkers related to brain injury. Front. Physiol. 9, 1367.
Egan, B., Sharples, A.P., 2023. Molecular responses to acute exercise and their relevance for adaptations in skeletal muscle to exercise training. Physiol. Rev. 103 (3), 2057–2170.
Ercan, Z., Deniz, G., Yentur, S.B., Arikan, F.B., Karatas, A., Alkan, G., Koca, S.S., 2023. Effects of acute aerobic exercise on cytokines, klotho, irisin, and vascular endothelial growth factor responses in rheumatoid arthritis patients. Ir. J. Med. Sci. 192 (1), 491–497.
Ergenc, I., Capar, E., Erturk, S.B., Bahramzade, G., Atalah, F., Kocakaya, D., Karakurt, S., Haklar, G., Odabasi, Z., 2023. Diagnostic performance of lactate dehydrogenase (LDH) isoenzymes levels for the severity of COVID-19. J. Med. Biochem. 42 (1), 16–26.
Feng, L.T., Chen, Z.N., Bian, H., 2024. Skeletal muscle: molecular structure, myogenesis, biological functions, and diseases. MedComm 5 (7), e649.
Forcina, L., Miano, C., Pelosi, L., Musarò, A., 2019. An overview about the biology of skeletal muscle satellite cells. Curr. Genom. 20 (1), 24–37.
Forman, S., Mela, K., 2025. Manual soft-tissue manipulation and its use in recovery, regeneration, and adaptation to exercise stress. Fundamentals of Recovery, Regeneration, and Adaptation to Exercise Stress: An Integrated Approach. Springer Nature Switzerland, Cham, pp. 597–632.
Fujiyoshi, H., Egawa, T., Kurogi, E., Yokokawa, T., Kido, K., Hayashi, T., 2022. TLR4-mediated inflammatory responses regulate exercise-induced molecular adaptations in mouse skeletal muscle. Int. J. Mol. Sci. 23 (3), 1877.
Galimov, A., Merry, T.L., Luca, E., Rushing, E.J., Mizbani, A., Turcekova, K., Hartung, A., Croce, C.M., Ristow, M., Krützfeldt, J., 2016. MicroRNA-29a in adult muscle stem cells controls skeletal muscle regeneration during injury and exercise downstream of fibroblast growth factor-2. Stem Cells 34 (3), 768–780.
Glancy, B., Kane, D.A., Kavazis, A.N., Goodwin, M.L., Willis, W.T., Gladden, L.B., 2021. Mitochondrial lactate metabolism: history and implications for exercise and disease. J. Physiol. 599 (3), 863–888.
Guzman, S.D., Brooks, S.V., 2025. Skeletal muscle innervation: reactive oxygen species as regulators of neuromuscular junction dynamics and motor unit remodeling. Free Radic. Biol. Med.
Haller, N., Blumkaitis, J.C., Strepp, T., Schmuttermair, A., Aglas, L., Simon, P., Neuberger, E., Kranzinger, C., Kranzinger, S., O'Brien, J., Ergoth, B., Raffetseder, S., Fail, C., Düring, M., Stöggl, T., 2022. Comprehensive training load monitoring with biomarkers, performance testing, local positioning data, and questionnaires - first results from elite youth soccer. Front. Physiol. 13, 1000898.
Hambright, W.S., Mu, X., Gao, X., Guo, P., Kawakami, Y., Mitchell, J., Mullen, M., Nelson, A.L., Bahney, C., Nishimura, H., Hellwinkel, J., Eck, A., Huard, J., 2023. The senolytic drug fisetin attenuates bone degeneration in the Zmpste24-/- Progeria mouse model. J. Osteoporos. 2023, 5572754.
Hansell, E.J., Reynolds, K.M., Škarabot, J., James, L.J., Clifford, T., Thorley, J., 2025. Urinary N-terminal titin fragment concentration as a non-invasive biomarker of exercise-induced muscle damage in males and females. Eur. J. Appl. Physiol. 1–13.
Harris-Love, M.O., Gollie, J.M., Keogh, J.W., 2021. Eccentric exercise: adaptations and applications for health and performance. J. Funct. Morphol. Kinesiol. 6 (4), 96.
He, Y., Wang, Q., Wu, H., Dong, Y., Peng, Z., Guo, X., Jiang, N., 2023. The role of IGF-1 in exercise to improve obesity-related cognitive dysfunction. Front. Neurosci. 17, 1229165.
Hendry, J.I., Erol, M.E., Layec, G., Debold, E.P., Tewari, S.G., Wallqvist, A., Pannala, V. R., 2025. A human skeletal muscle cross-bridge model to characterize the role of metabolite accumulation in muscle fatigue. Exp. Physiol.
Herzog, W., 2018. The multiple roles of titin in muscle contraction and force production. Biophys. Rev. 10 (4), 1187–1199.
Hill, J., Howatson, G., van Someren, K., Leeder, J., Pedlar, C., 2014. Compression garments and recovery from exercise-induced muscle damage: a meta-analysis. Br. J. Sports Med. 48 (18), 1340–1346.
Hong, W., Huang, W., 2025. The role of the creatine phosphate system in energy storage and release: from molecular mechanisms to physiological functions. J. Energy Biosci. 16.
Horgan, B.G., Halson, S.L., Drinkwater, E.J., West, N.P., Tee, N., Alcock, R.D., Chapman, D.W., Haff, G.G., 2023. No effect of repeated post-resistance exercise cold or hot water immersion on in-season body composition and performance responses in academy rugby players: a randomised controlled cross-over design. Eur. J. Appl. Physiol. 123 (2), 351–359.
Howatson, G., Gaze, D., van Someren, K.A., 2005. The efficacy of ice massage in the treatment of exercise-induced muscle damage. Scand. J. Med. Sci. Sports 15 (6), 416–422.
Howatson, G., Van Someren, K.A., 2003. Ice massage: effects on exercise-induced muscle damage. J. Sports Med. Phys. Fit. 43 (4), 500–505.
Jeon, Y.K., Kwon, J.W., Jang, J., Choi, S.W., Woo, J., Cho, S.H., Yu, B.I., Chun, Y.S., Youm, J.B., Zhang, Y.H., Kim, S.J., 2022. Lower troponin expression in the right ventricle of rats explains interventricular differences in E-C coupling. J. Gen. Physiol. 154 (3), e202112949.
Ji, Y., Li, M., Chang, M., Liu, R., Qiu, J., Wang, K., Sun, H., 2022. Inflammation: roles in skeletal muscle atrophy. Antioxidants 11 (9), 1686.
Kamal, K.Y., Trombetta-Lima, M., 2025. Mechanotransduction and skeletal muscle atrophy: The interplay between focal adhesions and oxidative stress. Int. J. Mol. Sci. 26 (6), 2802.
Kano, Y., Sonobe, T., Inagaki, T., Sudo, M., Poole, D.C., 2012. Mechanisms of exercise-induced muscle damage and fatigue: Intracellular calcium accumulation. J. Phys. Fit. Sports Med. 1 (3), 505–512.
Kanzaki, K., Watanabe, D., Shi, J., Wada, M., 2022. Mechanisms of eccentric contraction-induced muscle damage and nutritional supplementations for mitigating it. J. Muscle Res. Cell Motil. 43 (3), 147–156.
Khetarpal, S.A., Li, H., Lerchenmüller, C., Rhee, J., Rosenzweig, A., 2025. Molecular mediators of the cardiac benefits of exercise. Circ. Res. 137 (2), 163–183.
Kim, M., Eo, H., Lim, J.G., Lim, H., Lim, Y., 2022. Can low-dose of dietary vitamin e supplementation reduce exercise-induced muscle damage and oxidative stress? A meta-analysis of randomized controlled trials. Nutrients 14 (8), 1599.
Kiriaev, L., Baumann, C.W., Lindsay, A., 2023. Eccentric contraction-induced strength loss in dystrophin-deficient muscle: Preparations, protocols, and mechanisms. J. Gen. Physiol. 155 (2), e202213208.
Kraemer, W.J., Bush, J.A., Wickham, R.B., Denegar, C.R., Gomez, A.L., Gotshalk, L.A., Sebastianelli, W.J., 2001. Continuous compression as an effective therapeutic intervention in treating eccentric-exercise-induced muscle soreness. J. Sport Rehabil. 10 (1), 11–23.
Krüger, M., Kötter, S., 2016. Titin, a central mediator for hypertrophic signaling, exercise-induced mechanosignaling and skeletal muscle remodeling. Front. Physiol. 7, 76.
Kumar, P., Rathee, R., Nara, K., Sirotariya, A.K., Sangwan, N., 2025. Quantifying muscle recovery: a scoping review of existing markers and measurement approaches. Pol. J. Sport Tour. 32 (2), 3–13.

Kusmierczyk, J., Wiecek, M., Bawelski, M., Szygula, Z., Rafa-Zablocka, K., Kantorowicz, M., Szymura, J., 2024. Pre-exercise cryotherapy reduces myoglobin and creatine kinase levels after eccentric muscle stress in young women. Front. Physiol. 15, 1413949.
Lazar, D.R., Lazar, F.L., Homorodean, C., Cainap, C., Focsan, M., Cainap, S., Olinic, D.M., 2022. High-sensitivity troponin: a review on characteristics, assessment, and clinical implications. Dis. Markers 2022 (1), 9713326.
Lecina, M., Castellar-Otín, C., García-Giménez, A., Pradas, F., 2024. Exertional rhabdomyolysis and ultra-trail races: a systematic review highlighting the significant impact of eccentric load. Muscles 3 (3), 242–258.
Li, D.C.W., Rudloff, S., Langer, H.T., Norman, K., Herpich, C., 2024. Age-associated differences in recovery from exercise-induced muscle damage. Cells 13 (3), 255.
Li, G., Shang, L., Wang, X., Zhang, L., Zhao, Y., Ni, W., Bai, X., Liu, J., 2025. Whey protein mitigates oxidative stress injury and improves protein synthesis in mouse skeletal muscle by regulating the SIRT1/Nrf2/HO-1 axis and AMPK/TSC2/mTOR/4EBP1 pathway. J. Food Sci. 90 (7), e70286.
Lin, W., Song, H., Shen, J., Wang, J., Yang, Y., Yang, Y., Lin, R., 2023. Functional role of skeletal muscle-derived interleukin-6 and its effects on lipid metabolism. Front. Physiol. 14, 1110926.
Lindsay, A., Abbott, G., Ingalls, C.P., Baumann, C.W., 2021. Muscle strength does not adapt from a second to third bout of eccentric contractions: a systematic review and meta-analysis of the repeated bout effect. J. Strength Cond. Res. 35 (2), 576–584.
Long, Y., Wang, P., Lei, J., Su, B., Wei, Q., Liu, X., 2025. Mechanical signaling: molecular mechanisms, biological functions, diseases, and therapeutic targets. MedComm 6 (12), e70523.
Luo, W., Zhang, H., Wan, R., Cai, Y., Liu, Y., Wu, Y., Shang, X., 2024. Biomaterials-based technologies in skeletal muscle tissue engineering. Adv. Healthc. Mater. 13 (18), 2304196.
Luti, S., Modesti, A., Modesti, P.A., 2020. Inflammation, peripheral signals and redox homeostasis in athletes who practice different sports. Antioxidants 9 (11), 1065.
Lygate, C.A., 2024. Maintaining energy provision in the heart: the creatine kinase system in ischaemia–reperfusion injury and chronic heart failure. Clin. Sci. 138 (8), 491–514.
Ma, X., Liu, B., Jiang, Z., Rao, Z., Zheng, L., 2025. Physical exercise: a promising treatment against organ fibrosis. Int. J. Mol. Sci. 26 (1), 343.
Magherini, F., Fiaschi, T., Marzocchini, R., Mannelli, M., Gamberi, T., Modesti, P.A., Modesti, A., 2019. Oxidative stress in exercise training: the involvement of inflammation and peripheral signals. Free Radic. Res. 53 (11-12), 1155–1165.
Margaritelis, N.V., Theodorou, A.A., Baltzopoulos, V., Maganaris, C.N., Paschalis, V., Kyparos, A., Nikolaidis, M.G., 2015. Muscle damage and inflammation after eccentric exercise: can the repeated bout effect be removed? Physiol. Rep. 3 (12), e12648.
Markus, I., Constantini, K., Hoffman, J.R., Bartolomei, S., Gepner, Y., 2021. Exercise-induced muscle damage: Mechanism, assessment and nutritional factors to accelerate recovery. Eur. J. Appl. Physiol. 121 (4), 969–992.
Matthews, M.J., Kanungo, S., Baker, R.J., Kenter, K., 2024. Exercise physiology: a review of established concepts and current questions. Physiologia 4 (2), 202–212.
Mavropalias, G., Boppart, M., Usher, K.M., Grounds, M.D., Nosaka, K., Blazevich, A.J., 2023. Exercise builds the scaffold of life: muscle extracellular matrix biomarker responses to physical activity, inactivity, and aging. Biol. Rev. 98 (2), 481–519.
McFarlin, B.K., Venable, A.S., Henning, A.L., Sampson, J.N.B., Pennel, K., Vingren, J.L., Hill, D.W., 2016. Reduced inflammatory and muscle damage biomarkers following oral supplementation with bioavailable curcumin. BBA Clin. 5, 72–78.
Methenitis, S., Stergiou, I., Antonopoulou, S., Nomikos, T., 2021. Can exercise-induced muscle damage be a good model for the investigation of the anti-inflammatory properties of diet in humans? Biomedicines 9 (1), 36.
Michalak, K.P., Michalak, A.Z., 2025. Understanding chronic inflammation: couplings between cytokines, ROS, NO, Cai 2+, HIF-1α, Nrf2 and autophagy. Front. Immunol. 16, 1558263.
Michelucci, A., Liang, C., Protasi, F., Dirksen, R.T., 2021. Altered Ca^{2+} handling and oxidative stress underlie mitochondrial damage and skeletal muscle dysfunction in aging and disease. Metabolites 11 (7), 424.
Moore, E., Fuller, J.T., Bellenger, C.R., Saunders, S., Halson, S.L., Broatch, J.R., Buckley, J.D., 2023. Effects of cold-water immersion compared with other recovery modalities on athletic performance following acute strenuous exercise in physically active participants: a systematic review, meta-analysis, and meta-regression. Sports Med. 53 (3), 687–705.
Morgan, J.E., Zammit, P.S., 2010. Direct effects of the pathogenic mutation on satellite cell function in muscular dystrophy. Exp. Cell Res. 316 (18), 3100–3108.
Mu, L., Song, H., Jin, M., Li, K., Guo, Y., Jiang, N., 2025. Role of the admission muscle injury indicators in early coagulopathy, inflammation and acute kidney injury in patients with severe multiple injuries. World J. Emerg. Surg. 20 (1), 19.
Mukund, K., Subramaniam, S., 2020. Skeletal muscle: A review of molecular structure and function, in health and disease. Wiley Interdiscip. Rev. Syst. Biol. Med. 12 (1), e1462.
Nakhostin-Roohi, B., Nasirvand Moradlou, A., Mahmoodi Hamidabad, S., Ghanivand, B., 2016. The effect of curcumin supplementation on selected markers of delayed onset muscle soreness (DOMS). Ann. Appl. Sport Sci. 4 (2), 25–31.
Nash, D., Hughes, M.G., Butcher, L., Aicheler, R., Smith, P., Cullen, T., Webb, R., 2023. IL-6 signaling in acute exercise and chronic training: potential consequences for health and athletic performance. Scand. J. Med. Sci. Sports 33 (1), 4–19.
Neuhaus, P., Oustanina, S., Loch, T., Krüger, M., Bober, E., Dono, R., Zeller, R., Braun, T., 2003. Reduced mobility of fibroblast growth factor (FGF)-deficient myoblasts might contribute to dystrophic changes in the musculature of FGF2/FGF6/mdx triple-mutant mice. Mol. Cell. Biol. 23 (17), 6037–6048.
Nicol, L.M., Rowlands, D.S., Fazakerly, R., Kellett, J., 2015. Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS). Eur. J. Appl. Physiol. 115 (8), 1769–1777.
Nikolaidis, M.G., Jamurtas, A.Z., Paschalis, V., Fatouros, I.G., Koutedakis, Y., Kouretas, D., 2008. The effect of muscle-damaging exercise on blood and skeletal muscle oxidative stress: magnitude and time-course considerations. Sports Med. 38 (7), 579–606.
Nitti, M., Marengo, B., Furfaro, A.L., Pronzato, M.A., Marinari, U.M., Domenicotti, C., Traverso, N., 2022. Hormesis and oxidative distress: pathophysiology of reactive oxygen species and the open question of antioxidant modulation and supplementation. Antioxidants 11 (8), 1613.
Nyawo, T.A., Pheiffer, C., Mazibuko-Mbeje, S.E., Mthembu, S.X.H., Nyambuya, T.M., Nkambule, B.B., Sadie-Van Gijsen, H., Strijdom, H., Tiano, L., Dludla, P.V., 2021. Physical exercise potentially targets epicardial adipose tissue to reduce cardiovascular disease risk in patients with metabolic diseases: oxidative stress and inflammation emerge as major therapeutic targets. Antioxidants 10 (11), 1758.
Odriozola, A., Tirnauca, C., Corbi, F., González, A., Álvarez-Herms, J., 2025. Physiological responder profiles and fatigue dynamics in prolonged cycling. J. Funct. Morphol. Kinesiol. 10 (4), 472.
O'Riordan, S.F., McGregor, R., Halson, S.L., Bishop, D.J., Broatch, J.R., 2023. Sports compression garments improve resting markers of venous return and muscle blood flow in male basketball players. J. Sport Health Sci. 12 (4), 513–522.
Owens, D.J., Twist, C., Cobley, J.N., Howatson, G., Close, G.L., 2019. Exercise-induced muscle damage: What is it, what causes it and what are the nutritional solutions? Eur. J. Sport Sci. 19 (1), 71–85.
Özdemir, K., Demir, Y., 2025. Phenolic compounds in exercise physiology: dual role in oxidative stress and recovery adaptation. Food Sci. Nutr. 13 (8), e70714.
Özturk, N., Ceylan, H., Demir, Y., 2024. The hepatoprotective potential of tannic acid against doxorubicin-induced hepatotoxicity: insights into its antioxidative, anti-inflammatory, and antiapoptotic mechanisms. J. Biochem. Mol. Toxicol. 38 (8), e23798.
Pang, B.P.S., Chan, W.S., Chan, C.B., 2021. Mitochondria homeostasis and oxidant/antioxidant balance in skeletal muscle—do myokines play a role? Antioxidants 10 (2), 179.
Peake, J.M., Neubauer, O., Della Gatta, P.A., Nosaka, K., 2017. Muscle damage and inflammation during recovery from exercise. J. Appl. Physiol.
Perandini, L.A., Chimin, P., Lutkemeyer, D.D.S., Câmara, N.O.S., 2018. Chronic inflammation in skeletal muscle impairs satellite cells function during regeneration: can physical exercise restore the satellite cell niche? FEBS J. 285 (11), 1973–1984.
Powers, S.K., Jackson, M.J., 2008. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. Physiol. Rev. 88 (4), 1243–1276.
Primer, K.R., Psaltis, P.J., Tan, J.T., Bursill, C.A., 2020. The role of high-density lipoproteins in endothelial cell metabolism and diabetes-impaired angiogenesis. Int. J. Mol. Sci. 21 (10), 3633.
Puranik, N., Parihar, A., Raikwar, J., Khandia, R., 2021. Lactate dehydrogenase a potential diagnostic biomarker for cancer-a review of literature. Biomed. J. Sci. Tech. Res. 38 (3), 30426–30432.
Qi, C., Song, X., Wang, H., Yan, Y., Liu, B., 2022. The role of exercise-induced myokines in promoting angiogenesis. Front. Physiol. 13, 981577.
Qian, Z., Ping, L., Xuelin, Z., 2023. Re-examining the mechanism of eccentric exercise-induced skeletal muscle damage from the role of the third filament, titin. Biomed. Rep. 20 (1), 14.
Radak, Z., Zhao, Z., Koltai, E., Ohno, H., Atalay, M., 2013. Oxygen consumption and usage during physical exercise: the balance between oxidative stress and ROS-dependent adaptive signaling. Antioxid. Redox Signal. 18 (10), 1208–1246.
Radišić Biljak, V., Lazić, A., Nikler, A., Pekas, D., Saračević, A., Trajković, N., 2025. Post-exercise creatine kinase variability: a literature review. Biochem. Med. 35 (2), 186–200.
Rai, A., Bhati, P., Pal, S., Anand, P., 2024. Repeated bout effect and muscle damage at variable eccentric exercise intensities in active young men: a longitudinal repeated measures investigation. Comp. Exerc. Physiol. 20 (3), 243–255.
Ramirez-Sanchez, I., Navarrete-Yañez, V., Ramirez, L., Galera, L., Mendez-Bolaina, E., Najera, V., Ceballos, G., Villarreal, F., 2024. Restorative effects of (+)-epicatechin in a rodent model of aging induced muscle atrophy: underlying mechanisms. Food Funct. 15 (7), 3669–3679.
Rasmussen, M., Jin, J.P., 2021. Troponin variants as markers of skeletal muscle health and diseases. Front. Physiol. 12, 747214.
Rodriguez, J., Vernus, B., Chelh, I., Cassar-Malek, I., Gabillard, J.C., Hadj Sassi, A., Seiliez, I., Picard, B., Bonnieu, A., 2014. Myostatin and the skeletal muscle atrophy and hypertrophy signaling pathways. Cell. Mol. life Sci. CMLS 71 (22), 4361–4371.
Ruas, C.V., Taylor, J.L., Latella, C., Haff, G.G., Nosaka, K., 2025. Neuromuscular characteristics of eccentric, concentric and isometric contractions of the knee extensors. Eur. J. Appl. Physiol. 125 (3), 671–686.
Salem, A., Ben Maaoui, K., Jahrami, H., AlMarzooqi, M.A., Boukhris, O., Messai, B., Clark, C.C.T., Glenn, J.M., Ghazzaoui, H.A., Bragazzi, N.L., Ammar, A., Trabelsi, K., Chtourou, H., 2024. Attenuating muscle damage biomarkers and muscle soreness after an exercise-induced muscle damage with Branched-Chain Amino Acid (BCAA) supplementation: a systematic review and meta-analysis with meta-regression. Sports Med. Open 10 (1), 42.
Sanjabi, S., Zenewicz, L.A., Kamanaka, M., Flavell, R.A., 2009. Anti-inflammatory and pro-inflammatory roles of TGF-β, IL-10, and IL-22 in immunity and autoimmunity. Curr. Opin. Pharmacol. 9 (4), 447–453.
Satija, S., Mitchell, T.W., Anthony, R., Peoples, G.E., Sampson, J.A., 2025. From strain to repair: a targeted review of lipid mediators driving the inflammatory cascade following exercise: S. Satija et al. Sports Med. 1–15.

Schwiete, C., Roth, C., Mester, J., Broich, H., Behringer, M., 2025. Overlaps of skeletal muscle fatigue and skeletal muscle damage: the muscle injury continuum. Sports Med. Open 11 (1), 73.
Sharma, B., Dabur, R., 2020. Role of pro-inflammatory cytokines in regulation of skeletal muscle metabolism: a systematic review. Curr. Med. Chem. 27 (13), 2161–2188.
Sheikh, M.S., Kashani, K.B., 2025. Beyond creatinine: new methods to measure renal function? Eur. J. Intern. Med. 134, 17–24.
Sikder, M.M., Li, X., Akumwami, S., Labony, S.A., 2025. Reactive oxygen species: role in pathophysiology, and mechanism of endogenous and dietary antioxidants during oxidative stress. Chonnam Med. J. 61 (1), 32.
Sil, R., Chakraborti, A.S., 2025. Major heme proteins hemoglobin and myoglobin with respect to their roles in oxidative stress–a brief review. Front. Chem. 13, 1543455.
Sinaga, F.A., Sinaga, R.N., Manalu, N., 2021. Effect of Giving Beetroot Juice During Submaximal Exercise Against Muscle Damage. In: Journal of Physics: Conference Series, 1819. IOP Publishing, 012013.
Sipos, A., Varga, D., Pál, E., 2025. The diagnostic potential of urinary titin fragment in neuromuscular diseases. Int. J. Mol. Sci. 26 (19), 9652.
Smith, T.T.G., Gallagher, S., 2018. Impact of loading and work rest intervals on muscle micro-trauma. Int. J. Ind. Ergon. 66, 161–168.
Smith, C., Kruger, M.J., Smith, R.M., Myburgh, K.H., 2008. The inflammatory response to skeletal muscle injury: illuminating complexities. Sports Med. 38 (11), 947–969.
Smith, J.A., Murach, K.A., Dyar, K.A., Zierath, J.R., 2023. Exercise metabolism and adaptation in skeletal muscle. Nat. Rev. Mol. Cell Biol. 24 (9), 607–632.
Snijders, T., Verdijk, L.B., van Loon, L.J., 2009. The impact of sarcopenia and exercise training on skeletal muscle satellite cells. Ageing Res. Rev. 8 (4), 328–338.
Sonkodi, B., 2025. Delayed-onset muscle soreness begins with a transient neural switch. Int. J. Mol. Sci. 26 (5), 2319.
Soori, R., Amini, A.A., Choobineh, S., Eskandari, A., Behjat, A., Ghram, A., Voltarelli, F. A., 2022. Exercise attenuates myocardial fibrosis and increases angiogenesis-related molecules in the myocardium of aged rats. Arch. Physiol. Biochem. 128 (1), 1–6.
Steen, E.H., Wang, X., Balaji, S., Butte, M.J., Bollyky, P.L., Keswani, S.G., 2020. The role of the anti-inflammatory cytokine interleukin-10 in tissue fibrosis. Adv. Wound care 9 (4), 184–198.
Stemmerik, M.G., Barthel, B., Andersen, N.R., Skriver, S.V., Russell, A.J., Vissing, J., 2025. Universal proteomic signature after exercise-induced muscle injury in muscular dystrophies. Ann. Clin. Transl. Neurol. 12 (5), 998–1011.
Stožer, A., Vodopivc, P., Bombek, L.K., 2020. Pathophysiology of exercise-induced muscle damage and its structural, functional, metabolic, and clinical consequences. Physiol. Res. 69 (4), 565.
Su, Y., Su, Z., 2025. Impact of exercise on immune cell infiltration in muscle tissue: implications for muscle repair and chronic disease. Clin. Exp. Med. 25 (1), 306.
Sundari, L.P.R., Ar, N.L.K.A., 2022. Regular physical exercise increase of Growth hormone (GH) and Insulin-like growth factor-1 (IGF-1) activity in elderly improve the aging process and quality of life: A mini review. Biomed. Pharmacol. J. 15 (2), 883–890.
Tabone, M., 2025. Muscle mechanics in metabolic health and longevity: the biochemistry of training adaptations. BioChem 5 (4), 37.
Talebi, S., Mohammadi, H., Zeraattalab-Motlagh, S., Arab, A., Keshavarz Mohammadian, M., Ghoreishy, S.M., Djafarian, K., 2024. Nutritional interventions for exercise-induced muscle damage: an umbrella review of systematic reviews and meta-analyses of randomized trials. Nutr. Rev. 82 (5), 639–653.
Terrell, K., Choi, S., Choi, S., 2023. Calcium's role and signaling in aging muscle, cellular senescence, and mineral interactions. Int. J. Mol. Sci. 24 (23), 17034.
Tinsley, G.M., Gann, J.J., Huber, S.R., Andre, T.L., La Bounty, P.M., Bowden, R.G., Gordon, P.M., Grandjean, P.W., 2017. Effects of fish oil supplementation on postresistance exercise muscle soreness. J. Diet. Suppl. 14 (1), 89–100.
Tokuda, N., Himori, K., Ashida, Y., Naito, A., Yamauchi, N., Niibori, A., Yamada, T., 2025. The contralateral repeated bout effect is not caused by adaptations in skeletal muscle. J. Appl. Physiol. 139 (3), 605–615.
Tornero-Aguilera, J.F., Jimenez-Morcillo, J., Rubio-Zarapuz, A., Clemente-Suárez, V.J., 2022. Central and peripheral fatigue in physical exercise explained: a narrative review. Int. J. Environ. Res. Public Health 19 (7), 3909.
Torres-Ruiz, J., Alcalá-Carmona, B., Alejandre-Aguilar, R., Gómez-Martín, D., 2023. Inflammatory myopathies and beyond: the dual role of neutrophils in muscle damage and regeneration. Front. Immunol. 14, 1113214.
Tsuchiya, Y., Yanagimoto, K., Nakazato, K., Hayamizu, K., Ochi, E., 2016. Eicosapentaenoic and docosahexaenoic acids-rich fish oil supplementation attenuates strength loss and limited joint range of motion after eccentric contractions: a randomized, double-blind, placebo-controlled, parallel-group trial. Eur. J. Appl. Physiol. 116 (6), 1179–1188.
Tu, H., Li, Y.L., 2023. Inflammation balance in skeletal muscle damage and repair. Front. Immunol. 14, 1133355.
Valle, X., Til, L., Drobnic, F., Turmo, A., Montoro, J.B., Valero, O., Artells, R., 2014. Compression garments to prevent delayed onset muscle soreness in soccer players. Muscles Liga tendons J. 3 (4), 295.
Vieira, A., Siqueira, A., Ferreira-Junior, J., et al., 2016. The effect of water temperature during cold-water immersion on recovery from exercise-induced muscle damage. Int. J. Sports Med. 37 (12), 937–943.
Vo, H.V.T., Nguyen, Y.T., Kim, N., Lee, H.J., 2023. Vitamin A, D, E, and K as matrix metalloproteinase-2/9 regulators that affect expression and enzymatic activity. Int. J. Mol. Sci. 24 (23), 17038.
Wang, K., Gan, M., Lei, Y., Liao, T., Li, J., Niu, L., Shen, L., 2025. Perspectives on mitochondrial dysfunction in the regeneration of aging skeletal muscle. Cell. Mol. Biol. Lett. 30 (1), 94.
Wang, L., Li, Y., Wang, X., Wang, P., Essandoh, K., Cui, S., Huang, W., Mu, X., Liu, Z., Wang, Y., Peng, T., Fan, G.C., 2020. GDF3 protects mice against sepsis-induced cardiac dysfunction and mortality by suppression of macrophage pro-inflammatory phenotype. Cells 9 (1), 120.
Wang, F., Wang, X., Liu, Y., Zhang, Z., 2021. Effects of exercise-induced ROS on the pathophysiological functions of skeletal muscle. Oxid. Med. Cell. Longev. 2021 (1), 3846122.
Wang, L., Yang, K., Xie, X., Wang, S., Gan, H., Wang, X., Wei, H., 2025. Macrophages as multifaceted orchestrators of tissue repair: bridging inflammation, regeneration, and therapeutic innovation. J. Inflamm. Res. 8945–8959.
Wang, K., Zhang, T., Dong, Q., Nice, E.C., Huang, C., Wei, Y., 2013. Redox homeostasis: the linchpin in stem cell self-renewal and differentiation. Cell Death Dis. 4 (3) e537-e537.
Washington, T.A., Schrems, E.R., 2025. Skeletal muscle damage and inflammation. Skelet. Muscle. Plast. Degener. Epigenet. 185–212.
Wertheimer, V., Antekolovic, L., Matkovic, B.R., 2018. Muscle damage indicators after land and aquatic plyometric training programmes. Monte J. Sports Sci. Med. 7 (1), 13–19.
Wozniak, A.C., Kong, J., Bock, E., Pilipowicz, O., Anderson, J.E., 2005. Signaling satellite-cell activation in skeletal muscle: markers, models, stretch, and potential alternate pathways. Muscle Nerve 31 (3), 283–300.
Xu, J., Zhang, J., Sang, K., 2025. Mechanisms of the biological response cascade to exercise-induced stress: a comprehensive review. Front. Sports Act. Living 7, 1691779.
Yamada, T., Ashida, Y., Tatebayashi, D., Himori, K., 2019. Myofibrillar function differs markedly between denervated and dexamethasone-treated rat skeletal muscles: role of mechanical load. PLoS One 14 (10), e0223551.
Yasul, Y., Yılmaz, B., Yasul, M.E., Şenel, Ö., Çınar, V., 2024. Recovery response of coenzyme Q10 to exercise-related physiological muscle damage, inflammation and oxidative stress: a systematic review. Turk. J. Kinesiol. 10 (1), 48–60.
Yoshida, T., Delafontaine, P., 2020. Mechanisms of IGF-1-mediated regulation of skeletal muscle hypertrophy and atrophy. Cells 9 (9), 1970.
Zarezadehmehrizi, A., Hong, J., Lee, J., Rajabi, H., Gharakhanlu, R., Naghdi, N., Azimi, M., Park, Y., 2021. Exercise training ameliorates cognitive dysfunction in amyloid beta-injected rat model: possible mechanisms of Angiostatin/VEGF signaling. Metab. brain Dis. 36 (8), 2263–2271.
Zhang, X., Zhang, D., Zhang, Y., Wang, J., Lu, J., 2025. Restoration of skeletal muscle function via mesenchymal stem cells: mechanistic insights and therapeutic advances in myasthenia gravis. Front. Cell Dev. Biol. 13, 1658062.
Zhao, J., Du, X., Fang, W., Zhu, H., Yue, B., 2025. Architecture and molecular machinery of skeletal myofibers: a systematic review of the structure–function relationships. Front. Cell Dev. Biol. 13, 1602607.
Zhu, Y., Chang, B., Pang, Y., Wang, H., Zhou, Y., 2023. Advances in hypoxia-inducible factor-1 α stabilizer deferoxamine in tissue engineering. Tissue Eng. Part B Rev. 29 (4), 347–357.
Zoladz, J.A., Grandys, M., Smeda, M., Kij, A., Kurpinska, A., Kwiatkowski, G., Karasinski, J., Hendgen-Cotta, U., Chlopicki, S., Majerczak, J., 2024. Myoglobin deficiency impairs maximal oxygen uptake and exercise performance: a lesson from Mb-/- mice. J. Physiol. 602 (5), 855–873.