

# A systematic review of the integration of molecular biomarkers and anthropometric parameters for monitoring fatigue and inflammation in athletes

Revisión sistemática de biomarcadores moleculares y parámetros antropométricos para monitorear fatiga e inflamación en atletas

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#### **Abstract**

Introduction: Fatigue and inflammation are key physiological processes that modulate both recovery and performance outcomes in athletes. Nevertheless, existing monitoring strategies are not typically designed to incorporate molecular and anthropometric markers, which limits their specificity and application in sports settings.

Objective: To critically appraise recent evidence on the integration of molecular biomarkers and anthropometric parameters for the assessment of inflammation and fatigue in athletes. Methodology: According to PRISMA 2020 guidelines, systematic searching was conducted in the Web of Science, ScienceDirect, and PubMed databases. A total of 47 included studies from peer-reviewed, English-language articles with human athletes and reporting both molecular and anthropometric data.

Results: The review documented associations between body composition and biomarkers of muscle fatigue, inflammation, endocrine control, immune defense, and metabolism. Significant signaling cascades such as nuclear factor kappa B, phosphoinositide-3-kinase/protein kinase B, and the hypothalamic-pituitary-adrenal axis were commonly involved. Greater muscle mass supports better recovery, whereas higher fat mass increases inflammation and metabolic risk. Discussion: Combining these biomarkers with anthropometric values increases precision in physiological assessment and reduces misclassification risks, particularly in highly trained subjects. This review promoted a two-stranded monitoring strategy—encompassing molecular and morphological measures—to support personalized training, nutrition, and recovery planning.

Conclusions: The combination of multiple biomarkers and anthropometric analysis presents a promising paradigm for individualized monitoring with significant implications for precision training and recovery protocols in sport science.

#### **Keywords**

Anthropometric; athletes; biomarkers; fatigue; inflammation.

#### Resumen

Introducción: La fatiga y la inflamación son procesos fisiológicos clave que afectan la recuperación y el rendimiento en atletas. Sin embargo, las estrategias actuales de monitoreo no suelen integrar marcadores moleculares y antropométricos, lo que limita su aplicabilidad en el ámbito deportivo.

Objetivo: Evaluar críticamente la evidencia reciente sobre la integración de biomarcadores moleculares y parámetros antropométricos para evaluar la inflamación y la fatiga en atletas.

Metodología: Siguiendo las directrices PRISMA 2020, se realizó una búsqueda sistemática en Web of Science, ScienceDirect y PubMed. Se incluyeron 47 estudios revisados por pares en inglés, realizados en atletas humanos, que informaron datos moleculares y antropométricos.

Resultados: Se identificaron correlaciones entre composición corporal y biomarcadores de fatiga muscular, inflamación, regulación endocrina, inmunidad y metabolismo. Se observaron comúnmente cascadas de señalización significativas, como el factor nuclear kappa B, la fosfatidilinositol-3-quinasa/cinasa dependiente de fosfatidilinositol y el eje hipotálamo-hipófisis-adrenal. Mayor masa muscular favorece la recuperación; mayor grasa corporal se asocia con mayor inflamación y riesgo metabólico.

Discusión: La combinación de biomarcadores y parámetros antropométricos mejora la precisión del monitoreo fisiológico, especialmente en atletas entrenados. Se propone una estrategia dual que integre indicadores moleculares y morfológicos.

Conclusiones: El análisis conjunto de biomarcadores y medidas antropométricas representa un enfoque prometedor para el monitoreo individualizado en la ciencia del deporte.

#### Palabras clave

Antropométricos; atletas; biomarcadores; fatiga; inflamación.





#### Introduction

In sports, inflammation and muscle fatigue are common phenomena in athletes, particularly following excessive training. If not properly addressed, these conditions may impair performance and increase the risk of long-term damage (Halson, 2014; Saw et al., 2016; Jaspers et al., 2017). Early detection and a better understanding of how the body responds to training load have become central in coaching practice and athlete management. Although symptoms such as pain and fatigue are observable, they don't necessarily reflect the actual underlying physiological state.

To monitor performance and physical effort, coaches often rely on tools like GPS tracking, perceived exertion scores (RPE), and heart rate variability (HRV). Although useful, they mainly measure external workload or subjective effort. Without indicators of internal physiological response, risks related to fatigue, illness, or overtraining may go unnoticed (Buchheit, 2014; Plews et al., 2012; Meeusen et al., 2013; Halson, 2014). To bridge this gap, scientists have turned their attention more towards biological markers. Commonly used biomarkers include creatine kinase (CK), interleukin-6 (IL-6), C-reactive protein (CRP), cortisol, and secretory immunoglobulin A (s-IgA) to assess physiological stress and immune status (Podgórski et al., 2021; Soler-López et al., 2024; Slimani et al., 2025). These markers yield useful important internal data that may not be detected by conventional monitoring systems. Interpretation is influenced by hydration, sampling time, and body composition (Miloski et al., 2016; Saw et al., 2016; Haller et al., 2023).

Physical features such as muscle-to-fat ratio, somatotype, and lean mass distribution appear to influence how biomarkers respond to exercise stimuli. For example, hormones and cytokines like Insulin-Like Growth Factor-1 (IGF-1), IL-6, and cortisol may vary in concentration based on fat-free mass (FFM) or aerobic fitness level (McFadden et al., 2020; Peake et al., 2017; Bessa et al., 2016). In addition, metabolic biomarkers such as fat-mass (FM), leptin-to-adiponectin ratio (L/A), and Growth Differentiation Factor 15 (GDF-15) are implicated in inflammation processes and cardiovascular disease risk reversal processes (Tarabeih et al., 2024).

Integrating molecular biomarkers with anthropometric measures enables individualized training based on each athlete's physiological profile. Longitudinal changes in biomarkers relative to body composition and somatotype remain incompletely understood, despite known effects of season and playing position (Lee et al., 2017; Soler-López et al., 2024). Notably, Alves et al. (2021) findings indicated that changes in the intensity of training induced the decrease in fat-mass and increase in vVO<sub>2</sub>max, further confirming the interdependence between the anthropometric variables and the adaptive physiological response. Understanding biomarker–anthropometry interactions is increasingly relevant across performance levels.

While recent studies have also examined the connection between molecular biomarkers and physical parameters of athletes, the majority of studies prefer to treat these areas separately. Investigations that consider both the molecular and the anthropometric parameters in tracking fatigue, recovery, and performance are still relatively rare. Accordingly, this review adopts an integrative scope: while we highlight GDF-15 and the L/A ratio, we also synthesize evidence on established biomarkers of muscle fatigue, inflammation, endocrine regulation, immune status, and metabolism, together with anthropometric measures such as FFM, FM to weight ratio, and total body water (TBW). We use a five-domain framework and our inclusion criteria required at least one molecular biomarker and one anthropometric measure per study, which aligns the introduction, methods, and results. Rather than treating these indices as static values, we emphasize their dynamic links with training load, fatigue accumulation, and recovery over time.





#### Method

### Study Design

We used the PRISMA method to guide our literature search and selection (Page et al., 2021). Articles were collected from PubMed, Web of Science, and ScienceDirect using keywords like biomarkers, fatigue, inflammation, body composition, and training load. After removing duplicates, we screened the titles and abstracts, then reviewed the full texts of studies that matched our criteria.

#### Eligibility Criteria

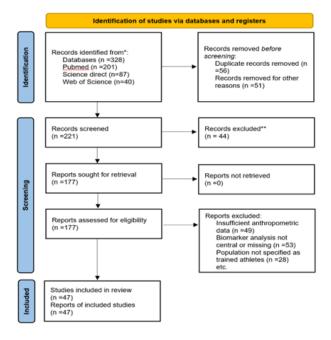
We included peer-reviewed English language studies (2011–2025) indexed in PubMed, Web of Science, or ScienceDirect that reported at least one molecular biomarker and one anthropometric measure in trained or elite athletes. Observational and interventional designs were eligible; sport and sex were unrestricted. We excluded non-athlete or clinical populations, non-English, animal studies, conference abstracts, non-indexed records, and studies lacking either data type.

Anthropometry included FFM, FM% or FM to weight ratio, body mass index (BMI), TBW, and when available waist circumference (WC), waist to height ratio (WHtR), and somatotype. These variables were prespecified because adiposity, muscle mass, and hydration modify inflammatory tone, fatigue risk, and measured concentrations (Frühbeck et al., 2019; Pérez Pérez et al., 2020; Baird et al., 2012; Saw et al., 2016; Haller et al., 2023; Ashwell & Gibson, 2016).

#### **Procedure**

A total of 328 records were initially retrieved from PubMed (n = 201), ScienceDirect (n = 87), and Web of Science (n = 40). After removing duplicates and performing an initial screening of titles and abstracts based on relevance and eligibility, 177 studies remained for full-text evaluation. Upon detailed assessment, 47 studies met the inclusion criteria and were selected for the final systematic review. The selection process was summarized in a PRISMA 2020 flow diagram (see Figure 1), which visually describes the number of records identified, screened, excluded, and included in this review.

Figure 1. PRISMA Flow Diagram Of The Article Selection Process







#### Results

This systematic review synthesized evidence on interactions between molecular biomarkers and anthropometric parameters related to fatigue, inflammation, and training adaptation in athletes. To provide a coherent synthesis, we grouped biomarkers into five functional domains by biological function and monitoring utility (Haller et al., 2023; Lee et al., 2017). Muscle fatigue markers CK, LDH, and myoglobin reflect sarcolemmal strain and mechanical load (Baird et al., 2012; Souglis et al., 2018). Inflammation markers CRP, IL-6, TNF- $\alpha$ , and GDF-15 reflect cytokine activity and systemic inflammatory tone (Bessa et al., 2016; Wahl et al., 2021; Tarabeih et al., 2024). Endocrine markers cortisol, IGF-1, GH, and testosterone reflect stress and the anabolic or catabolic balance (Meeusen et al., 2013; McFadden et al., 2020). Immune marker s-IgA reflects mucosal immune surveillance (Meeusen et al., 2013). Metabolic markers BUN, glucose, and albumin or total protein reflect energy availability and protein turnover (Banfi et al., 2012; Wahl et al., 2021). Consistent with our inclusion criteria, all studies reported at least one molecular biomarker and one anthropometric measure. We focused on anthropometry that plausibly links to these pathways. FFM can shift baseline enzyme concentrations and load tolerance (Baird et al., 2012; Haller et al., 2023). FM and central adiposity ((WC/WHtR) raise inflammatory tone and relate to insulin resistance risk (Bessa et al., 2016; Wahl et al., 2021; Ashwell and Gibson, 2016; Frühbeck et al., 2019). TBW and hydration status influence circulating concentrations (Miller et al., 2019; Saw et al., 2016). Table 1 summarizes these integrated relationships and their relevance for monitoring strategies in sport science.

Table 1. Integrated Overview of Molecular Biomarkers, Associated Physiological Pathways, Anthropometric Influences, And Practical Monitoring Implications

Author (Year)	Biomarker	Biomarker Category	Biological Function	Anthropometric Influence	Pathways Involved	Effect/ Response	Implication / Monitoring Strategy
(Baird et al., 2012; Souglis et al., 2018)	СК	Muscle Fatigue	Muscle damage indicator	Baseline CK levels are higher in individuals with greater muscle mass, particularly in males	Cell membrane disruption, calcium influx	Elevated CK may reflect normal adaptation or indicate muscle fatigue if excessive; interpretation should be context- dependent.	Monitor for eccentric-induced muscle damage; adjust recovery periods.
(Lee et al., 2017; Souglis et al., 2018)	LDH	Muscle Fatigue	Tissue breakdown indicator	Levels increase with greater FFM and eccentric load; associated with body size and training intensity.	Anaerobic glycolysis	tissue breakdown and training intensity; typically reflects muscle fatigue under eccentric loading	Track post-training recovery and muscle stress; useful after eccentric loading.
(Haller et al., 2023; Saita et al., 2023)	Myoglobin		Oxygen-binding protein in skeletal and cardiac muscle; released into circulation following muscle fiber damage	Higher concentrations observed in individuals with larger muscle mass or following eccentric exercise.	and calcium-	Myoglobin increases acutely after intense activity or eccentric exercise; indicates muscle damage or normal recovery depending on training load.	Use for acute muscle injury detection; helpful after high-intensity sessions.
(Docherty et al., 2022; Waśkiewicz et al, 2025)	IL-6	Inflammation	Inflammatory cytokine	Negatively associated with muscle glycogen and positively influenced by higher FM.	NF-ĸB activation, immune signaling	IL-6 initiates inflammatory signaling and rises with low muscle glycogen or higher fat mass; a marker of physiological inflammation.	Track inflammatory response; adapt nutrition and rest strategies.
(Bessa et al., 2016; Wahl et al., 2021)	CRP	Inflammation	Acute-phase inflammatory protein	Levels correlate positively with FM and central adiposity (WC/WHtR).	IL-6 induction of hepatic synthesis	CRP indicates systemic inflammation and tends to be higher with increased fat mass or central adiposity; used to	Assess systemic inflammation; monitor recovery sufficiency.





						assess recovery status.	
(Tarabeih et al., 2024)	TNF-α	Inflammation	Pro- inflammatory cytokine	Higher in individuals with increased FM; inversely associated with muscle mass and physical fitness.	Activates NF- κB/MAPK; triggers inflammation and muscle catabolism	Elevated TNF-α promotes chronic inflammation and may impair muscle recovery;	Identify chronic inflammation risk; personalize training intensity.
(Soler-López et al., 2024; Tarabeih et al., 2024)	GDF-15	Inflammation	Stress-induced cytokine involved in inflammation, cellular stress response, and energy metabolism regulation.	Elevated in those with greater FM or metabolic stress; linked to altered body composition.	TGF-β superfamily signaling, SMAD- dependent pathway	GDF-15 reflects metabolic and inflammatory stress; elevation may signal overtraining or disrupted recovery in individuals with higher FM.	Flag overtraining or mitochondrial stress; guide workload reduction.
(Meeusen et al., 2013)	Cortisol	Hormonal	Stress hormone	Higher in individuals with low FFM; varies by sex.	HPA axis	Cortisol increases with stress and lower FFM; chronic elevation can lead to fatigue or maladaptation if unmanaged.	Evaluate stress and catabolism; adjust training load and rest.
(McFadden et al., 2020)	IGF-1	Hormonal	Anabolic growth factor	Positively correlated with FFM and cardiorespiratory fitness (VO <sub>2</sub> max).	PI3K-Akt-mTOR pathway		Monitor muscle adaptation; guide long-term strength planning.
(Meeusen et al., 2013; Bessa et al., 2016; McFadden et al., 2020)	GH	Hormonal	Promotes tissue growth, protein synthesis, and lipolysis; supports recovery and adaptation.		JAK/STAT pathway, MAPK	•	Support in anabolic monitoring; adapt strength training plans.
(Meeusen et al., 2013; McFadden et al., 2020)	Testosterone	Hormonal	Anabolic hormone involved in muscle growth, protein synthesis, and recovery processes.	Higher in individuals with greater FFM and muscle mass; levels influenced by sex and training.	Androgen receptor signaling pathway	Testosterone supports hypertrophy and recovery; low levels may suggest overtraining or catabolic stress in athletes.	Assess anabolic status; balance training-recovery ratio.
(Meeusen et al., 2013; Slimani et al., 2025)	s-IgA	Immunological	Mucosal immunity	Lower in individuals with reduced FFM and under high training stress.	Immune mucosal secretion	Reduced s-IgA indicates compromised mucosal immunity; often observed in states of fatigue and elevated training stress.	Track mucosal immunity; prevent URTI risk with adjusted intensity.
(Meeusen et al., 2013; Slimani et al., 2025)	α-Amylase	Stress-related salivary biomarker (SNS activity marker)	Enzyme involved in carbohydrate digestion; also reflects autonomic (sympathetic) activity under stress	Potentially influenced by FM/FFM ratio and stress-related factors.	Sympathetic nervous system (SNS); salivary response to stress	α-Amylase levels reflect acute stress response; decrease during overtraining, indicating chronic fatigue or load mismanagement.	Evaluate acute stress; modify training environment and intensity.
(Banfi et al., 2012; Saw et al., 2016; Wahl et al., 2021; Haller et al., 2023)	BUN	Metabolic	Byproduct of protein metabolism; reflects protein catabolism and renal function.	Higher in those with low FFM or high protein intake; related to FFM/FM ratio.	breakdown;	Elevated BUN reflects protein breakdown or metabolic stress; high levels suggest poor recovery or dehydration.	Check protein catabolism and hydration; refine diet and rest.
(Zouhal et al, 2020; Wahl et	Glucose	Metabolic	Primary energy substrate; regulates	Varies with fat mass percentage,	Insulin signaling, AMPK pathway,	Glucose dysregulation may impair	Monitor energy status; ensure
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al., 2021; Cao et al., 2025;)			energy availability during exercise	BMI, and insulin sensitivity.	glucose transport (GLUT4)	performance and recovery; lower levels post- exercise more common in high- fat mass individuals.	proper fueling pre/post training.
(Banfi et al., 2012; Wahl et al., 2021)	Albumin / Total Protein	Metabolic	, ,	Lower in individuals with low BMI or muscle mass; influenced by hydration and protein intake.	Liver protein synthesis; regulated by inflammatory cytokines (e.g., IL-6, TNF-α); also influenced by insulin and nutritional signaling.	Low albumin/total protein indicates catabolic state or poor nutrition; stable levels reflect adequate recovery and hydration.	
(Friedman, 2011; Pérez-Pérez et al., 2020)	Leptin	Metabolic, pro- inflammatory adipokine	Regulates appetite and energy balance; pro- inflammatory signaling in high levels.	Levels increase with higher FM and BMI.	IAK/STAT NE.	Promotes low-grade systemic inflammation; impairs recovery if chronically elevated Leptin elevation reflects low-grade inflammation and poor recovery in athletes with high fat mass; a marker of energy imbalance.	Useful to assess energy availability and inflammation in athletes with excess fat mass
(Mallardo et al, 2023; Mallardo et al., 2024)	Adiponectin	Metabolic, Anti- inflammatory adipokine	Enhances insulin sensitivity; anti- inflammatory adipokine.	Decreased in individuals with higher FM and visceral adiposity.	AMPK, PPAR-α.	commonly seen with higher visceral adiposity.	Monitor anti- inflammatory status; adapt aerobic training focus.
(Agostinis- Sobrinho et al., 2022; Tylutka et al, I 2024; Lima et al., 2024; Tarabeih et al., 2024)	Leptin/Adiponectin Ratio	Marker of metabolic- inflammation balance	Reflects balance between pro- and anti- inflammatory adipokines		AMPK pathway, adipocytokine signaling	low VO <sub>2</sub> max;	Use as bio-marker to detect metabolic inflammation and guide nutrition/weight- management

### **Discussion**

This review demonstrates the value of integrating molecular biomarkers with anthropometric parameters to provide a more refined and individualized framework for monitoring fatigue, inflammation, and physiological adaptation in athletes. Conventional approaches often interpret biomarkers in isolation, without accounting for the modifying effects of body composition. Empirical examples support this point. CRP shows a positive correlation with FM and central fat deposition, suggesting an increased level of inflammation (Bessa et al., 2016; Wahl et al., 2021; Herawati et al., 2025). Levels of s-IgA are generally diminished during intense training and in athletes who have less FFM, which links to a heightened likelihood of upper respiratory infections (Meeusen et al., 2013). We analyze biomarkers in conjunction with body measurements and categorize our findings into five areas.

Muscle fatigue biomarkers including CK, LDH, and myoglobin generally change based on exercise intensity, mode of exercise, and individual changes in muscle mass or composition. Consequently, CK shows the impact of stress on the sarcolemma along with the body's adaptive mechanisms instead of being a direct measure of fatigue. CK concentrations frequently elevate following eccentric workouts, especially in those athletes who have a greater amount of lean body mass. In the case of well-conditioned athletes, a short-term rise in CK levels generally signifies a response to eccentric strain, as long as recovery is sufficient (Souglis et al., 2018; Sole et al., 2021; Baird et al., 2012). In professional football, a systematic review identified creatine kinase as the most frequently used biochemical marker after matches and closely related to the load imposed by the game (de Lima e Silva et al., 2024). These findings support CK





as a context-dependent indicator of load and recovery. LDH also reflects increased levels with severe or anaerobic activity, especially in sportsmen engaged in intensive strength training or increased muscle mass (Souglis et al., 2018; Lee et al., 2017). Myoglobin typically increases after short, high-intensity exercise and is not necessarily accompanied by structural fiber disruption or altered membrane permeability. Higher myoglobin peaks have also been noted in high-lean body mass volunteers or subjects with repeated eccentric movement (Haller et al., 2023; Saita et al., 2023). Whereas it would be expected for increases to be transient with training, chronically elevated values, particularly in individuals with reduced muscle stores or impaired recovery, may reflect poor repair or enhanced susceptibility to muscle injury. When interpreted alongside body composition data, myoglobin tracking could provide more context-specific insights into fatigue and help guide recovery plans.

Inflammatory responses in athletes can be assessed by several key biomarkers, such as IL-6, CRP, TNFα, and GDF-15. IL-6 is typically released during muscular contractions, especially when glycogen stores are diminished and fat mass is elevated. Increased IL-6 may reflect both impaired energy metabolism and heightened inflammatory activity (Docherty et al., 2022; Waśkiewicz et al., 2025). CRP, a liver-synthesized acute phase protein, is mainly controlled by IL-6 and represents a marker of low-grade systemic inflammation. In athletes, central adiposity indexed by WC or WHtR is associated with higher CRP and slower recovery (Ashwell & Gibson, 2016; Frühbeck et al., 2019; Wahl et al., 2021). Similarly, TNF-α, a central pro-inflammatory cytokine, has also been discovered thigher concentrations in individuals with greater FM and lower muscle mass. Long-term high TNF-α can hinder muscle repair and amplify fatigue, particularly during high-intensity training periodes (Tarabeih et al., 2024). GDF-15 functions as a cytokine that responds to stress and is a member of the TGF-β superfamily. It is regulated by cell stress response levels such as ATF4 and CHOP and regulated on the receptor GFRAL in the brainstem, which is of critical importance for energy regulation. In athletes, levels of GDF-15 are elevated with training and recovery stress levels and it is a prime exercise-induced inflammation and metabolic stress marker. In a clinical context, higher levels of GDF-15 are a predictor of type 2 diabetes and insulin resistance but will raise baseline levels in athletes without being a valid diagnostic tool. Athletes need to cross-reference the levels of GDF-15 with body fat percentage, muscle mass, and most recent training status. Temporary increases after exercise are typical, yet persistently elevated levels, particularly alongside increased fat mass or poor recovery, could suggest a lack of adequate adaptation (Soler-López et al., 2024; Tarabeih et al., 2024; Li et al., 2024; Wang et al., 2024; Chuang et al., 2025).

Hormonal markers such as cortisol, IGF-1, GH, and testosterone are also significantly associated with the body's adaptation to exercise stress as well as training recovery. All of these hormones have specific associations with body composition measurement such as muscle mass as well as body fat distribution. Cortisol is a catabolic stress hormone that would normally be increased in athletes with low FFM or chronic training stress state. Its increase is an indication of activation of the hypothalamic-pituitary-adrenal (HPA) axis, muscle protein breakdown, and immunosuppression—making it very significant tracking recovery in sport athletes prone to maladaptation (Meeusen et al., 2013). IGF-1 correlates positively with  $VO_2$ max, training load, and fat-free mass. Higher IGF-1 indicates a positive anabolic status and favorable muscular adaptation, whereas sustained low IGF-1 may reflect energy deficiency, excessive load, or catabolic stress (McFadden et al., 2020; Meeusen et al., 2013). GH stimulates IGF-1 by stimulating protein synthesis, growth of tissue, and lipid metabolism. GH release is usually inversely related to adiposity, and greater lean mass individuals are also found to have more intense GH response to exercise. They are all mediated through the GH/IGF-1 axis and critical molecular pathways like JAK/STAT and PI3K-Akt (Bessa et al., 2016; Meeusen et al., 2013).

Testosterone, another key anabolic hormone, is responsible for growth and adaptation of muscles at the level of physiological adaptation. Its concentration is generally connected with body composition, especially with FFM, and, depending on training load, sex, and day-night cycle. When testosterone drops while cortisol remains high, maladaptive responses to training should be suspected. This balance is often assessed through the testosterone-to-cortisol (T/C) ratio, which provides insight into anabolic–catabolic status and is useful for adjusting training intensity and recovery protocols (McFadden et al., 2020).

Immune function and stress biomarkers including s-IgA and salivary  $\alpha$ -amylase provide more accurate indications of physical stress and immune stress response in athletes. Monitoring some biomarkers over a period of time may give an early warning of overtraining or compromised immunity, especially when





combined with a concomitant shift in the anthropometric profile. s-IgA, one of the most common immune factors found on mucous surfaces like the respiratory tract, often declines in athletes with reduced FFM or insufficient recovery—conditions associated with increased risk of upper respiratory tract in-(Gleeson al., 2011; Meeusen et al., 2013; Slimani et Salivary α-amylase, a marker of sympathetic nervous system activity, increases with physical or psychologic stress. It increases after intense exercise and emotionally stressful challenges. Low  $\alpha$ -amylase values in the long term, however, indicate cumulative fatigue or recovery failure (Meeusen et al., 2013; Slimani et al., 2025).

Cumulatively, longitudinal monitoring of s-IgA and  $\alpha$ -amylase provide valuable insights on how the body manages physical stress and immune encounters. Such biomarkers can now be assessed through non-invasive sampling, their utility in athlete monitoring systems continues to gain attention. When interpreted alongside anthropometric data, the markers improve early detection of overtraining, personalized recovery planning, and long-term performance control. Molecular markers and body measurements serve as complementary tools. Molecular indicators reflect immediate physiological responses, while body composition offers the structural and hormonal framework that influences these responses. An increase in FFM can expand the availability of muscle enzymes and might raise baseline levels of CK without causing injury (Baird et al., 2012; Haller et al., 2023). Elevated FM and central obesity (WC/WHtR) are linked to chronic inflammation, increased levels of CRP, and an unfavorable ratio of leptin to adiponectin (Bessa et al., 2016; Wahl et al., 2021; Frühbeck et al., 2019). Analyzing both factors collectively minimizes errors in classification and enhances personalized thresholds.

Some of the metabolic markers like blood urea nitrogen (BUN), glucose, and albumin-to-total protein ratio can be used as predictors of the body's recovery and adaptation to exercise. A raised BUN following high-intensity exercise will generally be seen in individuals with low lean body mass or impaired recovery, suggestive of enhanced protein breakdown or impaired tissue repair (Saw et al., 2016; Wahl et al., 2021). Blood glucose is regulated, however, by a number of factors such as muscle mass, sensitivity to insulin, and overall body training stress. During the context of very prolonged or extremely intense exercise, glucose can fluctuate as part of the body's energy response. With the changes being permanent, they can also indicate an unfinished recovery state or deranged ability to adapt to impending physical stress (Zouhal et al., 2020; Wahl et al., 2021; Cao et al., 2025). Albumin and total protein values also change with the exercise- and stress-related fluid shifts. These, along with glucose and BUN, can offer a clearer understanding of an athlete's metabolic state and recovery capacity. Poor caloric intake during sustained exercise decreases blood glucose concentration greatly, making the athlete prone to hypoglycemia and decreasing physical performance. Athletes participating in decathlon events exhibit changes in blood glucose levels that align with when they consume food and how the competitions are scheduled (Yoshitake et al., 2024). This highlights the importance of aligning carbohydrate intake with training demands and tailoring strategies based on each athlete's distinct metabolic characteristics. On the contrary, stable glucose profiles in leaner individuals may indicate better metabolic adaptation. Continuous help fine-tune fueling strategies pre-Albumin and total proteins indicate nutritional status, hydration, and liver function. While mostly constant, slight decreases are possible with low BMI, non-recovery, or protein deficiency, while elevations can be indicative of plasma volume redistribution or acute-phase responses (Banfi et al., 2012; Wahl et al., 2021). Miller et al. (2019) highlighted that the shift of fluids secondary to exercise will impact concentration of serum albumin and that this needs to be interpreted relative to hydration status and change in plasma volume. The pro-inflammatory cytokines IL-6 and TNF-α were discovered to inhibit hepatic albumin synthesis, particularly in systemic stress. Albumin monitoring can thus be of benefit in assessment of long-term protein balance and adequacy of hydration. Combined, these metabolic markers provide functional feedback towards modulating training load, hydration, and dietary interventions, particularly repeated metabolic stress in endurance athletes.

The L/A ratio is recognized as a marker of metabolic stress, low-grade inflammation, and insulin resistance. Elevated ratios are commonly seen in individuals with greater fat mass and lower aerobic capacity, pointing to inefficient metabolic adaptation (Hu et al., 2023; Tarabeih et al., 2024; Tylutka et al., 2024). As fat stores expand, leptin levels rise and thus trigger inflammation signaling pathways such as JAK/STAT and NF- $\kappa$ B—particularly if increased over the long term (Friedman, 2011; Pérez Pérez et al., 2020). For endurance athletes, the concentration of leptin fluctuates with energy availability and training intensity cycles (de Assis & Murawska-Ciałowicz, 2023). Conversely, adiponectin improves insulin



sensitivity by activating pathways such as AMPK and PPAR- $\alpha$  but is decreased in individuals with more visceral fat (Mallardo et al., 2023; 2024). Although leptin and adiponectin have individually been the subject of many studies, the ratio provides an overall view of inflammation and metabolic response to exercise. This marker has been responsive to both training and nutrition interventions, therefore adequate for recovery status assessment (Senkus et al., 2022).

A high value of L/A is typically observed in people with greater fat mass and lower  $VO_2$ max, indicating poorer adaptation, particularly in those with inappropriate body composition (Agostinis-Sobrinho et al., 2022; Lima et al., 2024). A high L/A ratio may reflect poor metabolic adaptation and a reduced capacity to handle exercise-induced stress. Despite its relevance, this ratio is not yet commonly used in routine athlete assessments. Incorporating it into metabolic profiling could help detect early physiological strain and support more precise adjustments in training and recovery strategies (Frühbeck et al., 2019; Tylutka et al., 2024).

### Strengths and Limitations

A key strength of this review is its integrative perspective, merging the large repertoire of biomarkers of inflammation and immune markers through to hormonal markers and markers of fatigue and coupling them with generally accepted anthropometric parameters such as FFM, FM/WT ratio, and TBW. This integration offers more detailed information in terms of physiological adaptation occurring in athletes by relating biochemical outcomes with certain body composition traits. Furthermore, it offers a strong platform for the creation of evidence-based monitoring protocols that cater to the unique individual based on the optimization of athletic performance and the enhancement of recuperation efficacy (Lee et al., 2017).

Pairwise following ratios of biomarkers—such as leptin-to-adiponectin and GDF-15-to-leptin ratios—are capable of identifying changes in the body's metabolic and inflammatory condition, which individual markers might miss. In this review, we also outline a stepwise approach to interpreting these markers, which may help coaches and sport scientists make more informed decisions during athlete evaluations. However, some limitations should be noted. The heterogeneity of the studies incorporated on sport, stages of training, and sampling time generates variance that can affect study comparability. Furthermore, non-representation among female athletes, youth, and para-athletes limits generalizability of biomarker patterns. As Lee et al. (2017) clarified, these methodological differences complicate the inference of normative cutpoints. Subsequent research needs to use standardized protocols and longitudinal designs in order to establish sport-, sex-, and anthropometry-stratified biomarker baselines.

## Implications and Recommendations

This review emphasizes the importance of interpreting biomarkers alongside body composition metrics. Looking at molecular data in isolation may lead to misclassification, especially when distinguishing adaptive from maladaptive responses in elite athletes.

For practice, pair serial biomarker testing with routine anthropometry. Bioelectrical Impedance Analysis (BIA), Dual-Energy X-ray Absorptiometry (DEXA), or basic estimates of FFM can be useful when interpreting biomarker data, helping guide adjustments in training, recovery, and injury prevention strategies (Nana et al., 2015; Uchiyama et al., 2023).

Subsequent research ought to monitor the concurrent trajectories of biomarkers and anthropometric measurements throughout various training intervals. Collectively analyzed indicators can indicate early physiological stress such as overtraining, immunological dysregulation, or metabolic load. Of the above markers, GDF-15 is exercise and mitochondrial stress-sensitive: transient post-exercise increases are expected, but chronic increases, particularly with more FM or poorer recovery, would indicate underlying metabolic stress, e.g., impaired insulin sensitivity (Chuang et al., 2025; Wang et al., 2024). The L/A ratio serves as a marker for inflammation generated by obesity. Despite growing evidence suggesting a relationship between these indicators and adjustments along with body composition, their prevalent implementation in regular medical contexts remains limited; customized, long-term investigations are required to ascertain definitive thresholds for intervention (Frühbeck et al., 2019; Agostinis-Sobrinho et al., 2022).

Modern molecular biology has attached high significance to extracellular microRNAs (miRNAs) as markers of exercise responsiveness physiology. Present in body fluids such as plasma-derived vesicles and



sweat, miRNAs such as miR-21 and miR-146a are strongly associated with metabolic and immune pathways of whose levels of expression have been demonstrated to be altered following endurance-type exercise (Karvinen et al., 2020). As taken in conjunction with currently known markers such as leptin and CRP, such miRNA signatures would potentially add to understanding fatigue response and adaptation

Recent developments in wearable technology now allow real-time, non-invasive tracking of physiological markers such as cortisol, blood glucose, and electrolytes. Tools like sweat sensors and dried blood spot sampling are making it easier to track biomarkers in real-world settings, including during training or competition (Wang et al., 2022). When used alongside regular checks on body composition, this kind of monitoring gives coaches a clearer view of how athletes are recovering and whether adjustments in training might be needed.

### **Conclusions**

The review emphasizes a combination of molecular biomarkers and anthropometric findings to enhance monitoring in athletes. Modulations in biomarkers such as CK, IL-6, cortisol, IGF-1, TNF- $\alpha$ , CRP, and s-IgA such as CK, IL-6, cortisol, IGF-1, TNF- $\alpha$ , CRP, and s-IgA are always prone to body composition factors like FFM, FM, FM/weight ratio, and TBW. Failure to control for physical attributes will result in overestimation of recovery or performance status when interpreting the biomarkers. By integrating physiological and structural information, this study integrates the basis for individually tailored approaches within sports science. Future investigations should offer sport- and sex-specific reference ranges and incorporate larger populations to facilitate more accurate and relevant monitoring programs.

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