QUALITY IN SPORT
eISSN 2450-3118 · Open Access · Peer-reviewed
apcz.umk.pl/QS Nicolaus Copernicus University in Toruń

Cite as: KOLASA, Magdalena, KASTERKA, Natalia, KARBOWNIK, Liwia, FIGWER, Agnieszka, FIGWER, Krzysztof, DZITKOWSKA, Kinga, CZARNY, Norbert, BRONIECKA, Anna, ŚMIGIELSKI, Michał and GARBACIAK, Jędrzej. Integrated Monitoring of Hepcidin, Inflammatory Markers and Heart Rate Variability in Endurance Athletes: Implications for Early Detection of Non-Functional Overreaching - A Narrative Review. Quality in Sport. 2026;60:72789. https://doi.org/10.12775/QS.2026.60.72789

ARTICLE TIMELINE
Received: 28.05.2026. Revised: 23.06.2026. Accepted: 23.06.2026. Published: 27.06.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines: Medical Sciences; Health Sciences.
Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Nauki medyczne; Nauki o zdrowiu.

Integrated Monitoring of Hepcidin, Inflammatory Markers and Heart Rate Variability in Endurance Athletes: Implications for Early Detection of Non-Functional Overreaching - A Narrative Review

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Abstract

Background

Non-functional overreaching (NFOR) and overtraining syndrome (OTS) are maladaptive responses to excessive training load combined with insufficient recovery. Early diagnosis remains difficult because no single validated biomarker can reliably distinguish physiological fatigue from clinically significant maladaptation. Endurance athletes appear particularly vulnerable due to repeated exposure to high training volume, inflammatory activation and disturbances in iron metabolism.

Objective

The aim of this review was to evaluate the role of hepcidin, inflammatory markers and heart rate variability (HRV) as potential early indicators of non-functional overreaching in endurance athletes and to discuss the clinical relevance of integrated monitoring strategies.

Methods

A narrative review with systematic search elements was performed using PubMed/MEDLINE and scientific databases. The review included systematic reviews, meta-analyses, consensus statements and original studies published primarily between 2019 and 2026 focusing on endurance athletes, HRV, inflammation and iron metabolism.

Results

Available evidence suggests that HRV, particularly RMSSD, may reflect autonomic adaptation and recovery status during intensified training periods. Exercise-induced inflammatory activation, especially increased interleukin-6, contributes to post-exercise elevation of hepcidin, potentially reducing iron availability and impairing recovery capacity. However, HRV and inflammatory biomarkers are influenced by multiple physiological and environmental factors, limiting their isolated diagnostic value.

Conclusions
An integrated approach combining HRV trends, inflammatory markers and iron-regulatory biomarkers may improve early identification of athletes at risk of non-functional overreaching. Further prospective studies are required to validate combined monitoring strategies in endurance athletes.
Keywords: non-functional overreaching; overtraining syndrome; endurance athletes; hepcidin; inflammation; interleukin-6; heart rate variability; iron metabolism

Training load ↑ → Interleukin-6 ↑ → Hepcidin ↑ → Iron availability ↓ → Recovery impairment → HRV alteration → Increased risk of non-functional overreaching

Figure 1. Conceptual Pathway Linking Training Stress, Inflammation and Recovery Impairment

The conceptual model above illustrates the proposed interaction between excessive endurance training, inflammatory activation, altered iron metabolism and autonomic dysregulation in endurance athletes.

Graphical Abstract Description Excessive endurance training combined with insufficient recovery may trigger inflammatory activation, autonomic dysregulation and disturbances in iron metabolism. Increased interleukin-6 stimulates hepcidin synthesis, reducing iron availability and potentially impairing recovery capacity. Simultaneously, alterations in heart rate variability reflect autonomic imbalance associated with cumulative physiological stress. Integrated monitoring combining HRV trends, inflammatory markers and iron-related biomarkers may improve early identification of athletes at risk of non-functional overreaching.

1. Introduction

Contemporary endurance sport is associated with increasingly demanding training structures, dense competition calendars and constant pressure to optimize athletic performance. Over the past decades, advances in sports science and monitoring technologies have enabled athletes to tolerate substantially greater training loads than previously possible. Although properly planned overload remains a necessary component of adaptation, chronic imbalance between training stress and recovery may result in maladaptive physiological responses collectively described as non-functional overreaching (NFOR) and overtraining syndrome (OTS). These conditions continue to represent one of the most complex and controversial problems in contemporary sports medicine because their pathophysiology remains incompletely understood and no universally accepted diagnostic biomarker has yet been identified [1,2,29].

The distinction between functional overreaching and pathological maladaptation is particularly challenging in endurance athletes. Short-term fatigue and temporary reductions in performance are expected consequences of intensified training and may ultimately contribute to supercompensation and improved competitive outcomes. However, when excessive physiological stress is combined with insufficient recovery, inadequate nutritional support or chronic psychological burden, adaptive mechanisms may become progressively impaired. In such situations, athletes may experience prolonged fatigue, impaired exercise capacity, sleep disturbances, mood instability and persistent underperformance lasting weeks or months.

In clinical practice, early identification of maladaptation remains particularly challenging because many symptoms associated with NFOR resemble expected responses to intensified training periods. Temporary fatigue, reduced motivation or transient decreases in exercise tolerance are common even among well-adapted athletes undergoing heavy training blocks [1,2,29,30]. Traditional laboratory markers demonstrate limited specificity, while isolated physiological measurements often fail to reflect the complex multisystem nature of the condition. This likely explains why integrated monitoring strategies combining autonomic, inflammatory, metabolic and performance-related parameters have attracted increasing attention in sports medicine.

Among the physiological systems involved in training adaptation, autonomic nervous system regulation appears particularly important. Heart rate variability (HRV), reflecting beat-to-beat fluctuations in cardiac rhythm, has emerged as one of the most widely used non-invasive tools for monitoring recovery status and autonomic adaptation in athletes [3,4,34,35]. Reduced parasympathetic activity and altered HRV patterns have repeatedly been associated with increased physiological strain, inadequate recovery and maladaptive responses to training load [3,4,15,34,35]. At the same time, HRV interpretation remains difficult because autonomic regulation may be

influenced by sleep quality, psychological stress, hydration status, illness and environmental conditions. This may partially explain why some endurance athletes present substantial fatigue despite relatively stable laboratory findings and apparently normal training metrics.

At the same time, increasing evidence suggests that inflammatory activation and disturbances in iron metabolism may contribute significantly to impaired recovery and exercise maladaptation. Prolonged endurance exercise induces transient inflammatory responses involving cytokines such as interleukin-6 (IL-6), which play important metabolic and immunological roles during exercise adaptation. Under physiological conditions, these responses are considered beneficial and necessary for tissue remodeling and substrate mobilization. However, repeated exposure to excessive training stress may result in persistent inflammatory activation and impaired recovery processes.

Particular interest has recently been directed toward hepcidin, the principal regulator of systemic iron metabolism. Exercise-induced increases in IL-6 stimulate hepatic hepcidin synthesis, thereby reducing intestinal iron absorption and iron mobilization from storage sites [20,21,24]. Since iron availability is essential for oxygen transport, mitochondrial respiration and aerobic metabolism, disturbances in iron homeostasis may negatively influence endurance performance and recovery capacity. Endurance athletes appear especially vulnerable to exercise-related iron deficiency due to the combined effects of inflammatory regulation, exercise-induced hemolysis, gastrointestinal blood loss and high metabolic demand.

Despite the growing number of studies investigating HRV, inflammatory markers and hepcidin, currently available evidence remains insufficient to support the use of any isolated parameter as a reliable standalone biomarker of NFOR. This limitation likely reflects the multifactorial and highly individualized nature of maladaptation in endurance athletes. Available literature indicates that maladaptation likely develops through interaction between autonomic dysregulation, inflammatory signaling, metabolic stress and impaired recovery mechanisms rather than through isolated dysfunction within a single physiological pathway.

Therefore, the aim of the present review was to evaluate the potential role of heart rate variability, inflammatory response and hepcidin as early biomarkers of non-functional overreaching in endurance athletes and to discuss the clinical relevance of integrated monitoring strategies combining autonomic, inflammatory and iron-regulatory markers.

2. Methods

The review methodology was conceptually aligned with contemporary principles of narrative reviews incorporating systematic search elements and structured evidence synthesis. Although a formal PRISMA-guided systematic review was not performed, the literature search strategy and study selection process were designed to improve methodological transparency and reproducibility.

This article was designed as a narrative review with systematic search elements. The review question was formulated as follows:

Can the integration of hepcidin, inflammatory markers and heart rate variability improve early identification of non-functional overreaching in endurance athletes?

The review process was based on the PICO framework.

Population: endurance athletes exposed to high-volume aerobic training, including runners, cyclists, triathletes and swimmers.

Exposure and biomarkers: heart rate variability, hepcidin, inflammatory markers including interleukin-6 and C-reactive protein.

Comparison: normal training adaptation, functional overreaching, baseline values or recovered athletes.

Outcome: early detection of non-functional overreaching, impaired recovery, maladaptation and performance decline.

Literature searches were conducted using PubMed/MEDLINE and scientific databases. Search terms included combinations of the following keywords: “non-functional overreaching”, “overtraining syndrome”, “heart rate

variability", "HRV", "hepcidin", "interleukin-6", "inflammation", "iron metabolism", "training load", "recovery" and "endurance athletes".

Priority was given to systematic reviews, meta-analyses, consensus statements, scoping reviews and peer-reviewed original studies [1,3,29,30]. Older landmark publications were included when they provided important definitions or pathophysiological concepts related to NFOR and OTS.

Studies were excluded if they were unrelated to athletes, focused exclusively on non-exercise clinical populations or did not provide relevant information regarding autonomic regulation, inflammation, iron metabolism or exercise recovery.

3. Epidemiology and Clinical Significance of Non Functional Overreaching

Endurance sports continue to grow globally, resulting in increasing interest in training optimization and recovery monitoring. Competitive runners, cyclists, triathletes, rowers and swimmers are frequently exposed to large training volumes combined with high physiological stress. Although properly structured overload is necessary for performance adaptation, chronic imbalance between training stress and recovery may lead to maladaptation.

The prevalence of overtraining syndrome is difficult to estimate because diagnostic criteria remain inconsistent across studies. However, surveys conducted among endurance athletes suggest that a significant proportion of elite competitors experience symptoms consistent with non-functional overreaching at least once during their careers. Long-distance runners and cyclists appear particularly vulnerable due to the repetitive nature of endurance training and prolonged energy expenditure.

The clinical relevance of NFOR extends beyond reduced athletic performance. Athletes affected by maladaptation frequently report persistent fatigue, sleep disturbances, impaired concentration, reduced motivation, mood instability and increased susceptibility to infection. In severe cases, prolonged performance decline may result in interruption of competitive careers.

From a sports medicine perspective, one of the greatest challenges involves distinguishing physiological adaptation from maladaptive overload. Short-term fatigue is expected during heavy training periods and may even be necessary for supercompensation. Clinicians and coaches therefore need practical tools capable of identifying early warning signs before severe dysfunction develops. In practical sports medicine settings, transient fatigue and reduced HRV are frequently observed even in well-adapted athletes during intensive training blocks, which further complicates early differentiation between adaptive overload and clinically relevant maladaptation.

Several theoretical models have been proposed to explain the pathophysiology of NFOR and OTS. These include autonomic nervous system imbalance, chronic inflammatory activation, hypothalamic-pituitary adrenal axis dysregulation, glycogen depletion, oxidative stress and mitochondrial dysfunction [1,2,29,30]. Despite decades of research, no single mechanism has fully explained the syndrome.

Current evidence increasingly supports the concept that NFOR represents a multifactorial systemic process involving interaction between metabolic, immunological, endocrine and autonomic pathways [1,2,29,31]. This complexity makes isolated laboratory interpretation particularly difficult in endurance athletes. In real-world endurance training environments, athletes exposed to apparently similar workloads may demonstrate markedly different recovery dynamics and physiological responses. Modern monitoring strategies should therefore integrate multiple physiological domains rather than relying on single biomarkers alone.

4. Non-Functional Overreaching and Overtraining Syndrome

Functional overreaching represents a normal adaptive component of athletic training. Short-term reductions in performance during intensified training periods are expected and may lead to improved performance after recovery. However, when recovery is insufficient, the physiological stress associated with repeated training sessions may exceed the athlete's adaptive capacity.

Non-functional overreaching is characterized by persistent fatigue, prolonged performance impairment and incomplete recovery lasting from weeks to months. Overtraining syndrome represents a more severe condition associated with prolonged underperformance, psychological disturbances, recurrent infections and systemic dysregulation.

The pathophysiology of NFOR and OTS is complex and multifactorial. Proposed mechanisms include autonomic imbalance, chronic low-grade inflammation, neuroendocrine dysfunction, glycogen depletion, immune dysregulation and impaired mitochondrial adaptation.

The diagnosis of NFOR remains difficult because there is no single objective marker capable of distinguishing maladaptation from normal training fatigue. Consequently, modern sports medicine increasingly emphasizes longitudinal monitoring rather than isolated laboratory measurements.

Subjective symptoms such as sleep disturbances, increased perceived exertion, irritability and decreased motivation often precede objective performance decline. Therefore, integrated monitoring strategies combining physiological, biochemical and subjective markers may be particularly valuable.

5. Heart Rate Variability and Autonomic Adaptation in Endurance Athletes

Heart rate variability has become one of the most commonly utilized physiological tools for monitoring training adaptation and recovery status in endurance athletes. HRV reflects fluctuations in consecutive cardiac R-R intervals resulting from the interaction between sympathetic and parasympathetic branches of the autonomic nervous system. Because autonomic balance is closely associated with cardiovascular recovery, sleep quality, hormonal regulation and metabolic adaptation, disturbances in HRV have attracted considerable interest as potential indicators of maladaptive training responses.

Among the numerous HRV-derived parameters, the root mean square of successive differences (RMSSD) is currently regarded as the most practical index for athlete monitoring because it predominantly reflects parasympathetic modulation and demonstrates relatively good reproducibility under standardized conditions. Contemporary wearable technology has substantially increased the accessibility of HRV monitoring, allowing athletes and clinicians to obtain frequent measurements outside laboratory settings.

Studies performed in endurance athletes reported that intensified training periods may induce substantial alterations in autonomic regulation [3,4,10,12,35]. Nevertheless, the direction and magnitude of these responses remain inconsistent across studies, which further complicates clinical interpretation of HRV-derived parameters. In some athletes, excessive physiological stress is associated with reduced parasympathetic activity and decreased HRV, whereas others may develop paradoxical parasympathetic hyperactivity during chronic fatigue states. This heterogeneity suggests that autonomic responses to training load remain highly individualized and influenced by multiple physiological and psychological factors.

For this reason, interpretation of HRV requires considerable caution. Although reductions in vagally mediated HRV are frequently interpreted as indicators of insufficient recovery, similar alterations may also occur in response to psychological stress, travel fatigue, sleep disruption or acute illness. Isolated measurements possess limited clinical value because autonomic function may be affected by sleep deprivation, dehydration, travel fatigue, environmental temperature, illness, psychological stress and nutritional status. For this reason, repeated longitudinal assessment performed under standardized morning conditions appears more informative than isolated measurements. Single-point HRV values often provide only limited insight into the athlete's true recovery status.

Despite these methodological concerns, HRV continues to be regarded as one of the most practical non invasive tools currently available for monitoring recovery and autonomic adaptation in athletes. Its popularity results not only from physiological relevance but also from accessibility and ease of repeated measurement in real-world training environments. Several systematic reviews suggest that HRV-guided training approaches may improve individualization of training prescription and recovery management [3,10,25,35]. Moreover, reductions in HRV have repeatedly been associated with impaired recovery and increased physiological strain in endurance athletes.

HRV should therefore not be interpreted as an isolated diagnostic marker for NFOR or OTS. Although autonomic monitoring may provide valuable information regarding recovery status, the available literature suggests that HRV abnormalities alone are insufficient for differentiating physiological fatigue from clinically relevant maladaptation.

Rather, autonomic monitoring appears most clinically useful when integrated with subjective recovery measures, inflammatory biomarkers, training load quantification and performance assessment.

6. Autonomic Nervous System Dysregulation in Endurance Athletes

Autonomic nervous system dysfunction has long been considered one of the central physiological mechanisms potentially involved in the development of maladaptation and chronic fatigue in athletes exposed to excessive training stress. Early concepts of overtraining syndrome frequently divided athletes into so-called sympathetic and parasympathetic forms of overtraining. Although contemporary understanding recognizes that these categories are overly simplistic, autonomic imbalance remains an important theoretical framework for interpreting training-related fatigue and impaired adaptation.

The autonomic nervous system plays a critical role in cardiovascular regulation, endocrine signaling, thermoregulation, sleep architecture and metabolic adaptation. Consequently, chronic disturbances in autonomic balance may influence numerous physiological systems simultaneously. In endurance athletes, prolonged exposure to repetitive training stress may progressively alter autonomic responsiveness and impair recovery capacity.

One of the most frequently reported findings in athletes experiencing excessive fatigue involves altered parasympathetic modulation reflected by changes in HRV-derived indices. Reduced vagal activity may indicate inadequate recovery and increased sympathetic activation, particularly during periods of intensified training. However, chronic maladaptation may also produce paradoxical autonomic responses characterized by excessive parasympathetic predominance and reduced exercise responsiveness.

These observations emphasize that autonomic adaptation is highly dynamic and individualized. Factors such as age, sex, genetics, nutritional status, psychological stress and sleep quality may substantially influence autonomic responsiveness. Therefore, interpretation of autonomic markers requires individualized longitudinal analysis rather than rigid threshold-based classification.

Recent advances in wearable technology have substantially expanded the practical applications of autonomic monitoring. Modern chest straps, smartwatches and mobile applications allow collection of daily HRV measurements under real-world conditions [3,7,13]. This accessibility has contributed to increasing implementation of HRV-guided training strategies among endurance athletes.

Nevertheless, methodological limitations remain important. Measurement timing, body position, respiratory pattern, environmental conditions and device accuracy may all influence HRV-derived outcomes. Standardization of monitoring protocols therefore remains essential for improving data reliability and clinical interpretation.

Another important consideration involves the interaction between autonomic function and psychological stress. Athletes exposed to excessive competitive pressure, travel demands or academic and occupational stress may demonstrate altered HRV independently of physical training load. Consequently, autonomic monitoring should always be interpreted within broader psychosocial and physiological context.

Emerging evidence also suggests potential interactions between autonomic regulation and inflammatory signaling. Chronic physiological stress may contribute to simultaneous alterations in autonomic balance and inflammatory activation, further supporting the concept that NFOR represents a complex multisystem process.

Although autonomic monitoring cannot independently diagnose overtraining syndrome, HRV currently remains one of the most clinically useful non-invasive tools available for longitudinal recovery assessment in endurance athletes.

7. Inflammatory Response and Exercise-Induced Maladaptation

Inflammation plays an important role in exercise adaptation and tissue remodeling. Acute exercise induces transient increases in inflammatory mediators that contribute to tissue remodeling, metabolic regulation and recovery processes [11,20,21]. However, chronic excessive training load combined with insufficient recovery may contribute to prolonged inflammatory activation and impaired adaptation.

Interleukin-6 appears particularly important in endurance exercise physiology because it acts both as a metabolic regulator and inflammatory mediator. During prolonged endurance exercise, skeletal muscle releases IL-6 into circulation in response to glycogen depletion and cumulative metabolic stress.

Under physiological circumstances, transient increases in IL-6 contribute to substrate mobilization and adaptation. Nevertheless, repeated high-volume or high-intensity training sessions without sufficient recovery may contribute to persistent low-grade inflammatory activation.

Multiple investigations reported increased concentrations of inflammatory markers such as C-reactive protein, leukocyte count and tumor necrosis factor-alpha in athletes exposed to excessive physiological stress. However, interpretation of inflammatory biomarkers remains difficult because similar alterations may occur in response to infection, sleep deprivation, psychological stress or inadequate nutritional support.

Another important issue involves oxidative stress and immune adaptation. Prolonged endurance exercise may increase production of reactive oxygen species, particularly when recovery is inadequate or energy availability remains insufficient. Excessive oxidative stress may impair mitochondrial adaptation, recovery capacity and immune resilience.

Inflammatory activation should not be interpreted independently from autonomic and metabolic responses. In practice, maladaptation in endurance athletes likely reflects simultaneous interaction between inflammatory signaling, autonomic dysregulation, endocrine stress and impaired recovery [11,20,21,29].

For this reason, inflammatory biomarkers appear most clinically useful when interpreted together with HRV trends, training load analysis, subjective recovery assessment and markers of iron metabolism [3,11,20,31]. In practical athlete monitoring, isolated inflammatory-marker elevation often proves difficult to interpret without simultaneous analysis of recent training exposure and recovery status.

Table 1. Proposed Biomarkers for Monitoring Non-Functional Overreaching in Endurance Athletes

Domain	Marker	Clinical role	Limitation
Autonomic regulation	RMSSD	Parasympathetic recovery marker	Influenced by sleep and stress
Autonomic regulation	Resting heart rate	Reflects physiological strain	Low specificity
Inflammatory response	Interleukin-6	Exercise-related inflammatory signaling	Acute exercise effect
Inflammatory response	C-reactive protein	Systemic inflammation marker	Influenced by infection
Iron metabolism	Hepcidin	Regulates iron availability	Circadian variability
Iron metabolism	Ferritin	Reflects iron stores	Acute phase reactant

Iron metabolism	Transferrin saturation	Indicates circulating iron	Influenced by nutrition
Performance	Time trial performance	Sport-specific adaptation marker	Motivation dependent
Subjective recovery	Fatigue questionnaires	Assesses perceived recovery	Subjective variability

Table 1. Proposed Biomarkers Potentially Associated with Non-Functional Overreaching in Endurance Athletes Based on Available Evidence [3,11,18,20,24,31]

Current evidence suggests that combined interpretation of autonomic, inflammatory and iron-related biomarkers may provide greater clinical value than isolated assessment of single physiological parameters.

8. Inflammation, Recovery and Immune Function

Inflammation represents a physiological component of exercise adaptation and tissue remodeling. Acute endurance exercise induces transient increases in multiple cytokines and inflammatory mediators that contribute to metabolic regulation, immune signaling and recovery processes. Under normal circumstances, these responses are tightly controlled and ultimately support adaptation to repeated training stimuli.

Among the numerous cytokines involved in exercise physiology, interleukin-6 has attracted particular attention because of its dual metabolic and inflammatory functions. During prolonged exercise, skeletal muscle acts as an endocrine organ releasing IL-6 into circulation. Exercise-induced IL-6 release appears strongly associated with glycogen depletion, exercise duration and overall metabolic stress.

Physiological increases in IL-6 may support glucose regulation and substrate mobilization during exercise. However, repeated exposure to excessive training stress without sufficient recovery may contribute to persistent inflammatory activation and impaired recovery processes.

Several studies have reported increased concentrations of inflammatory markers such as CRP, TNF alpha and leukocyte count in athletes experiencing prolonged fatigue and underperformance [11,20,21]. Nevertheless, interpretation of inflammatory biomarkers remains difficult because these markers demonstrate limited specificity and may also increase in response to infection, injury, sleep deprivation and psychological stress.

Another important aspect involves oxidative stress and immune regulation. Prolonged endurance exercise may increase reactive oxygen species production, particularly when recovery is insufficient or nutritional support is inadequate. Excessive oxidative stress may impair mitochondrial adaptation, muscle recovery and immune resilience.

The relationship between inflammation and immune function in athletes remains highly complex and, in some areas, insufficiently understood. While moderate exercise is generally associated with favorable immunological adaptation, prolonged exposure to excessive physiological stress may produce the opposite effect and contribute to increased vulnerability to infection. Moderate exercise is generally associated with beneficial immunological adaptation, whereas chronic excessive training stress may increase susceptibility to upper respiratory tract infections and impair immune competence.

Low energy availability may further exacerbate inflammatory dysregulation. Athletes exposed to chronic caloric restriction or insufficient carbohydrate intake may demonstrate impaired recovery, increased cortisol concentrations and altered immune responses.

Environmental stressors also appear relevant. Heat exposure, altitude training and long-distance travel may all contribute to additional physiological strain and inflammatory activation.

Importantly, inflammatory responses should not automatically be interpreted as pathological. Acute transient increases in inflammatory mediators represent essential components of physiological adaptation. The primary clinical challenge therefore involves distinguishing adaptive inflammatory responses from maladaptive chronic activation.

For this reason, inflammatory biomarkers are unlikely to provide meaningful information when interpreted in isolation. Their clinical usefulness appears substantially greater when combined with autonomic monitoring, subjective recovery measures and longitudinal performance assessment.

9. Hepcidin and Iron Metabolism in Endurance Athletes

Hepcidin is a peptide hormone synthesized primarily by hepatocytes and currently recognized as the principal regulator of systemic iron metabolism. Its physiological function involves inhibition of ferroportin, the transmembrane protein responsible for iron export from enterocytes, macrophages and hepatocytes.

In endurance athletes, disturbances in iron regulation are clinically important because iron remains essential for oxygen transport, mitochondrial respiration and aerobic energy production. Exercise induced increases in IL-6 stimulate hepatic hepcidin synthesis, thereby linking inflammatory activation with altered iron availability [20,21,24].

Following prolonged endurance exercise, hepcidin concentrations may remain elevated for several hours. During this period, intestinal iron absorption and iron mobilization from storage sites become reduced. Repeated training sessions performed during periods of elevated hepcidin concentration may therefore contribute to progressive depletion of iron stores.

Endurance athletes appear particularly vulnerable to iron deficiency due to multiple interacting mechanisms, including exercise-induced hemolysis, gastrointestinal blood loss, sweating, urinary iron loss and high metabolic demand [18,19,22,23]. Female athletes may additionally experience menstrual iron losses, further increasing susceptibility to deficiency.

Functional iron deficiency may impair aerobic capacity, recovery and adaptation even before clinically significant anemia develops. Consequently, disturbances in iron metabolism may contribute substantially to fatigue and reduced exercise tolerance in athletes exposed to excessive training stress.

Interpretation of hepcidin remains complex because concentrations are influenced by circadian rhythm, baseline ferritin levels, inflammatory activity, nutritional status and recent exercise exposure. Therefore, isolated assessment of hepcidin possesses limited clinical value.

Available literature supports integrated evaluation of ferritin, transferrin saturation, hemoglobin, inflammatory markers and training context rather than reliance on isolated laboratory measurements [18,19,22,24].

The interaction between inflammatory signaling, iron metabolism and autonomic recovery represents one of the most promising areas of contemporary sports medicine research and may ultimately improve early identification of maladaptive responses to endurance training.

10. Clinical Implications of Iron Dysregulation in Endurance Athletes

Iron is essential for aerobic metabolism, oxygen transport and mitochondrial energy production. Consequently, disturbances in iron availability may significantly impair endurance performance, exercise tolerance and recovery capacity.

Endurance athletes appear particularly vulnerable to iron deficiency because repetitive prolonged exercise may increase iron loss through multiple physiological mechanisms. Exercise-induced hemolysis, gastrointestinal microbleeding, sweating and urinary iron loss have all been proposed as contributing factors. Female athletes may additionally experience menstrual iron losses, further increasing risk of deficiency.

In recent years, hepcidin has emerged as one of the most important regulators linking exercise-induced inflammation with systemic iron metabolism. Hepcidin is synthesized primarily by hepatocytes and functions through regulation of ferroportin, the principal iron export protein.

When hepcidin concentrations increase, intestinal iron absorption decreases and iron release from macrophages and hepatocytes becomes restricted. This may reduce iron availability for erythropoiesis and mitochondrial metabolism.

Exercise-induced hepcidin elevation appears strongly associated with IL-6 release following prolonged endurance exercise [20,21,24]. Peak hepcidin concentrations are generally observed several hours after exercise and may remain elevated during recovery periods.

The timing of training sessions and nutritional interventions may therefore influence long-term iron availability. Some authors have suggested that repeated exercise performed during periods of elevated hepcidin may impair dietary iron absorption and contribute to progressive depletion of iron stores.

Athletes with low baseline ferritin concentrations may demonstrate exaggerated physiological consequences of reduced iron availability. In practice, even mild functional iron deficiency may impair endurance performance and perceived recovery before clinically significant anemia becomes detectable.

Another clinically relevant issue involves the relationship between low energy availability and iron metabolism. Endurance athletes attempting to maintain low body mass or restrictive dietary strategies may simultaneously experience impaired recovery, hormonal disturbances and progressive reduction in iron availability. Athletes exposed to chronic caloric restriction may experience combined disturbances involving endocrine dysfunction, impaired recovery and altered iron regulation.

Interpretation of iron-related biomarkers remains clinically challenging because ferritin acts as an acute phase reactant and may increase during inflammation independently of actual iron stores. Similarly, hepcidin concentrations demonstrate circadian variability and are influenced by recent exercise exposure.

Interpretation of iron-related biomarkers therefore requires broader clinical context. Ferritin assessment alone may occasionally produce misleading conclusions, especially in athletes exposed to recent inflammatory stress or intensive training periods.

Despite these limitations, disturbances in iron metabolism may represent an important mechanistic component of maladaptation in endurance athletes. The interaction between inflammation, hepcidin regulation and impaired recovery continues to attract increasing scientific interest and may ultimately contribute to improved individualized athlete monitoring.

11. Integrated Monitoring Model

The concept of integrated athlete monitoring has gained increasing importance in contemporary sports medicine, particularly in endurance disciplines characterized by repetitive exposure to high physiological stress. Although numerous biomarkers associated with recovery and maladaptation have been investigated over recent decades, no single parameter has demonstrated sufficient sensitivity and specificity to independently identify non-functional overreaching or overtraining syndrome.

For this reason, current approaches increasingly emphasize multidimensional assessment combining physiological, biochemical, performance-related and subjective indicators. Available evidence suggests that interpretation of isolated laboratory abnormalities may be clinically misleading when broader recovery context is ignored. Similarly, transient autonomic suppression or inflammatory activation may occur during periods of intensified but physiologically adaptive training.

Multiple studies indicate that HRV monitoring may provide valuable information regarding autonomic recovery dynamics, particularly when repeated longitudinally under standardized conditions [3,4,10,25,34,35]. Nevertheless, the literature also indicates considerable interindividual variability in autonomic responses to training load. Some athletes demonstrate reduced vagally mediated HRV during periods of excessive fatigue, whereas others exhibit relatively stable autonomic patterns despite substantial physiological strain. This variability remains

one of the major reasons why interpretation of autonomic monitoring requires individualized clinical context rather than rigid universal thresholds.

Inflammatory markers demonstrate similar limitations. Acute increases in IL-6, CRP or leukocyte count are commonly observed following prolonged endurance exercise and do not necessarily indicate pathological maladaptation. However, persistent inflammatory activation combined with impaired recovery, increased fatigue and progressive underperformance may suggest cumulative physiological stress exceeding adaptive capacity.

In recent years, increasing attention has also been directed toward disturbances in iron metabolism, particularly exercise-induced alterations in hepcidin regulation. Several authors have suggested that repeated endurance exercise performed during periods of elevated hepcidin concentration may contribute to impaired iron availability and progressive reduction in exercise capacity [18,20,21,24]. Nevertheless, interpretation of hepcidin remains difficult because concentrations are influenced by circadian rhythm, recent exercise exposure, baseline ferritin levels and inflammatory activity.

Subjective recovery assessment also remains highly relevant in everyday athlete monitoring. In many real-world training environments, athletes report impaired recovery and reduced motivation before measurable deterioration becomes visible in laboratory or performance testing. In practical sports medicine settings, persistent fatigue, reduced motivation, impaired sleep quality and increased perceived exertion frequently precede measurable physiological deterioration. Some studies have even suggested that subjective monitoring tools may demonstrate greater practical sensitivity than selected objective biomarkers.

Another relevant issue involves the interaction between training load and psychosocial stress. Endurance athletes are often exposed not only to physical fatigue but also to academic pressure, travel burden, sleep disruption and competitive anxiety. These factors may independently influence autonomic regulation, inflammatory signaling and perceived recovery status.

Therefore, monitoring data should be interpreted longitudinally and always in relation to the individual athlete. It appears increasingly likely that NFOR represents a multifactorial process involving simultaneous dysregulation of several interconnected physiological systems.

From a practical perspective, the most useful strategy appears to involve combining HRV trends, inflammatory markers, iron-related biomarkers, subjective recovery assessment and performance testing rather than relying on a single parameter.

Table 2. Advantages and Limitations of Selected Biomarkers Used in Athlete Monitoring

Biomarker	Main advantages	Main limitations
HRV (RMSSD)	Non-invasive, easy daily monitoring, reflects autonomic recovery	Influenced by sleep, stress, illness and hydration
Interleukin-6	Reflects exercise-induced inflammatory signaling	Acute exercise substantially increases concentration
C-reactive protein	Widely available laboratory marker	Low specificity for maladaptation
Hepcidin	Provides insight into iron regulation	Circadian variability and limited standardization

Ferritin	Useful assessment of iron stores	Acute phase reactant influenced by inflammation
Subjective recovery questionnaires	Simple and inexpensive	Depend on athlete compliance and perception
Performance testing	Sport-specific evaluation of adaptation	Influenced by motivation and external conditions

Table 2. Advantages and Limitations of Selected Biomarkers Used in Endurance Athlete Monitoring Based on Available Evidence [3,11,18,20,24,31,35]

Available data indicate that no isolated biomarker provides sufficient diagnostic specificity for early detection of non-functional overreaching. Consequently, integrated monitoring strategies combining several physiological domains appear substantially more clinically useful.

12. Practical Applications in Sports Medicine and Athlete Monitoring

The growing availability of wearable technology and portable physiological monitoring systems has substantially changed contemporary athlete management. In previous decades, detailed assessment of autonomic regulation or recovery status was largely restricted to laboratory settings. Currently, endurance athletes are able to collect HRV measurements daily using commercially available devices integrated with mobile applications and cloud-based monitoring platforms.

Despite these technological advances, practical interpretation of physiological data remains challenging. One of the major problems observed in applied sports medicine involves excessive reliance on isolated numerical values without adequate consideration of broader clinical context. Recovery status cannot be reduced to a single parameter because adaptation to training is influenced simultaneously by sleep quality, nutritional status, psychological stress, environmental conditions and cumulative physiological load.

This issue becomes particularly relevant in endurance athletes participating in dense competition calendars or prolonged training camps. In such situations, transient autonomic suppression or elevated inflammatory markers may appear even in athletes who remain physiologically well adapted. Consequently, interpretation of monitoring data requires longitudinal perspective and familiarity with the athlete's individual physiological profile. Short-term physiological fluctuations are common during intensive training periods and do not necessarily indicate clinically significant maladaptation.

Subjective recovery measures remain highly valuable despite increasing emphasis on objective biomarker assessment [31,32]. Persistent fatigue, reduced motivation, irritability, impaired sleep quality and unusually high perceived exertion frequently precede measurable performance decline. Several authors have therefore suggested that subjective monitoring tools may, in some situations, demonstrate greater practical sensitivity than isolated physiological measurements.

Another clinically important consideration involves nutritional support and energy availability. Endurance athletes frequently attempt to optimize body composition while simultaneously maintaining high training volumes. However, chronic low energy availability may contribute to endocrine dysfunction, impaired immune adaptation, increased inflammatory stress and disturbances in iron metabolism.

The interaction between nutritional status and hepcidin regulation appears especially relevant in athletes at risk of iron deficiency. Current evidence suggests that timing of exercise sessions and iron intake may influence post-exercise iron absorption. Repeated training performed during periods of elevated hepcidin concentration may theoretically impair restoration of iron stores over time.

Female endurance athletes represent a particularly important subgroup because menstrual blood loss combined with high training loads may substantially increase the risk of iron deficiency and impaired recovery. Consequently, individualized monitoring strategies should consider sex-specific physiological differences and nutritional demands.

Environmental conditions may also influence recovery dynamics and physiological stress responses. Heat exposure, altitude training and frequent long-distance travel may independently alter autonomic regulation, inflammatory signaling and sleep quality. In elite athletes, these stressors frequently coexist with intensive competition schedules, creating substantial cumulative physiological burden.

Clinicians and coaches should recognize that abnormal biomarker patterns do not necessarily indicate pathological overtraining syndrome. Physiological adaptation to heavy training may temporarily produce findings resembling maladaptation. The central challenge therefore involves distinguishing transient adaptive responses from persistent dysfunction associated with inadequate recovery.

For this reason, integrated longitudinal monitoring strategies appear substantially more useful than isolated laboratory testing. Combining subjective assessment, training load analysis, HRV trends, inflammatory markers and iron-regulatory biomarkers may improve early recognition of maladaptive patterns before severe underperformance develops.

Future athlete monitoring systems will likely incorporate artificial intelligence-assisted analysis capable of integrating large volumes of physiological, biochemical and performance-related data [7,9,13]. Nevertheless, clinical interpretation and individualized assessment will probably remain essential components of sports medicine practice.

13. Limitations and Current Controversies

Despite substantial scientific interest in overtraining syndrome and non-functional overreaching, currently available evidence remains limited by considerable methodological heterogeneity. One of the principal difficulties involves the absence of universally accepted diagnostic criteria for NFOR, which significantly complicates comparison between studies and interpretation of reported findings.

Several authors have emphasized that many physiological responses traditionally associated with maladaptation may also occur during periods of intensified but functionally adaptive training [1,29,30]. Consequently, distinguishing between beneficial overload and pathological fatigue remains challenging in both research and clinical settings.

Another important limitation concerns the variability of autonomic responses observed in endurance athletes. Although reduced HRV has frequently been described in athletes exposed to excessive training stress, available studies demonstrate substantial interindividual differences. As reported by Bellenger et al. and later discussed in subsequent athlete-monitoring studies, some individuals may exhibit marked autonomic suppression, whereas others maintain relatively stable HRV values despite significant fatigue and underperformance.

Interpretation of inflammatory biomarkers appears similarly problematic. Acute exercise-induced increases in IL-6 and CRP represent normal physiological responses necessary for adaptation and tissue remodeling. However, persistent inflammatory activation may also reflect infection, inadequate nutritional support, sleep deprivation or psychosocial stress. For this reason, inflammatory markers demonstrate relatively limited specificity when analyzed independently.

The clinical relevance of hepcidin remains another area of ongoing discussion. Although exercise induced hepcidin elevation has repeatedly been observed following prolonged endurance exercise, the practical implications of transient increases in hepcidin concentration are not fully understood. Several studies suggest that repeated exercise sessions performed during periods of elevated hepcidin may impair long-term iron restoration; nevertheless, currently available evidence remains insufficient to establish standardized clinical recommendations.

Another issue frequently discussed in recent literature involves the reliability of wearable-derived physiological measurements. The growing popularity of mobile applications and commercial monitoring devices has

substantially increased accessibility of athlete monitoring. However, device accuracy, measurement standardization and data interpretation remain important concerns [7,13,25].

It should also be emphasized that many currently available studies involve relatively small athlete populations, short observation periods and heterogeneous training protocols. Female athletes continue to be underrepresented in certain areas of sports physiology research despite potentially increased susceptibility to disturbances in iron metabolism and low energy availability.

Finally, psychological and environmental factors remain difficult to quantify objectively. Competitive pressure, travel fatigue, academic stress and sleep disruption may significantly influence recovery dynamics and autonomic regulation independently of physical training load.

Taken together, these limitations suggest that maladaptation in endurance athletes should be interpreted as a multifactorial and highly individualized process rather than a condition identifiable through a single universal biomarker. One of the major practical challenges in athlete monitoring remains the substantial variability in recovery dynamics observed even among athletes exposed to apparently similar training loads.

Another important methodological limitation involves the relatively small sample sizes observed in many athlete-monitoring studies. Elite endurance athletes represent a difficult population to study under controlled conditions because training schedules, competition periods and recovery practices vary substantially between individuals and sports disciplines. Consequently, external validity and generalizability remain important concerns in contemporary sports physiology research [29,31,33].

14. Psychological Stress, Sleep Disturbance and Recovery Dynamics

Recovery processes in endurance athletes are influenced not only by physiological training load but also by psychological and behavioral factors. Increasing evidence suggests that sleep quality, emotional stress, academic or occupational burden and competition-related anxiety may significantly affect autonomic regulation, inflammatory signaling and perceived recovery.

Sleep appears particularly important because it directly influences hormonal regulation, immune adaptation, autonomic balance and tissue recovery [3,8,25,32]. Athletes exposed to insufficient sleep duration or fragmented sleep architecture may demonstrate impaired glucose metabolism, elevated cortisol concentrations and reduced parasympathetic activity. Several studies have also reported associations between poor sleep quality and reduced HRV in athletes undergoing intensive training [3,8,25,35].

Competitive endurance athletes are frequently exposed to cumulative psychological stressors unrelated to physical exercise itself. Travel demands, social pressure, academic responsibilities and expectations regarding performance may independently contribute to recovery impairment. In some athletes, psychological stress may even precede measurable physiological deterioration.

Another important consideration involves the interaction between sleep and inflammatory activation. Sleep restriction has been associated with increased inflammatory markers, including CRP and IL-6, potentially amplifying exercise-induced physiological stress. Consequently, chronic sleep disruption may contribute to impaired adaptation and increased perception of fatigue.

The practical interpretation of subjective fatigue remains complex because perceived exhaustion may result from both physiological and psychological mechanisms. Nevertheless, several studies have suggested that mood disturbance, reduced motivation and increased perceived exertion frequently precede objective reductions in athletic performance.

For this reason, athlete monitoring should not rely exclusively on laboratory biomarkers or wearable derived physiological data. Subjective recovery questionnaires, sleep assessment and psychosocial evaluation may provide clinically relevant information regarding recovery dynamics and cumulative stress exposure.

Nutrition also interacts strongly with sleep and recovery processes. Athletes exposed to low energy availability may experience disturbances in endocrine regulation, sleep quality and immune adaptation. Chronic caloric restriction may therefore amplify both inflammatory activation and autonomic dysregulation.

Environmental conditions may further complicate recovery management. Altitude exposure, heat stress and long-distance travel may impair sleep architecture, increase sympathetic activation and influence inflammatory responses. Elite endurance athletes often experience several of these stressors simultaneously during competition seasons.

Overall, non-functional overreaching should not be interpreted exclusively as a consequence of excessive physical training. Rather, maladaptation appears to result from interaction between physiological load, psychological stress, sleep quality, nutritional status and individual recovery capacity.

15. Emerging Technologies and Personalized Athlete Monitoring

Recent advances in sports science increasingly emphasize individualized athlete management supported by digital monitoring technologies and large-scale physiological data integration [3,7,9,13]. Contemporary athlete-monitoring systems increasingly combine wearable-derived physiological metrics with biochemical and subjective recovery indicators, allowing more comprehensive longitudinal assessment of adaptation dynamics. Wearable systems capable of continuous heart rate, sleep and recovery assessment are now widely accessible in both elite and recreational endurance sport.

This technological transition has substantially changed the practical approach to recovery monitoring. Historically, assessment of training adaptation relied primarily on coach observation, subjective fatigue and sport-specific performance testing. Although these methods remain clinically valuable, modern athlete monitoring increasingly incorporates continuous physiological measurements capable of detecting subtle changes in recovery dynamics.

Heart rate variability represents one of the most widely implemented wearable-derived physiological markers in contemporary endurance sport. However, future monitoring systems will likely integrate multiple interacting variables simultaneously, including sleep quality, respiratory rate, movement variability, skin temperature, biochemical markers and psychological stress assessment.

Another rapidly developing area involves artificial intelligence-assisted analysis of physiological trends. Machine learning algorithms may eventually allow identification of maladaptive recovery patterns before clinically significant performance decline develops. Such systems could potentially integrate longitudinal HRV trends, inflammatory responses, training load distribution and nutritional variables into individualized predictive models. However, currently available evidence remains insufficient to support widespread independent clinical implementation of fully automated athlete-monitoring systems.

Nevertheless, substantial methodological and ethical limitations remain. The accuracy of commercially available wearable devices varies considerably, and many algorithms currently lack independent clinical validation. Large volumes of physiological data may also become difficult to interpret without appropriate clinical context and individualized assessment. Excessive dependence on wearable-derived metrics without broader physiological interpretation may paradoxically increase uncertainty rather than improve athlete management.

Another important issue involves data privacy and athlete autonomy. Continuous monitoring systems collect extensive physiological and behavioral information, including sleep patterns, recovery status and psychological responses. Managing these data responsibly is becoming an increasingly important challenge in modern sports medicine.

Future monitoring strategies may also incorporate molecular and genomic biomarkers. Recent research has explored the role of metabolomics, proteomics and transcriptomic profiling in exercise adaptation and fatigue assessment. Although these technologies currently remain primarily research-oriented, they may eventually improve understanding of individual susceptibility to maladaptation.

The interaction between autonomic regulation, inflammatory signaling and iron metabolism appears particularly promising for development of multidimensional monitoring models. Rather than searching for a single universal biomarker, future approaches will likely focus on identifying individualized physiological patterns associated with impaired adaptation and recovery.

Another emerging direction involves sex-specific sports physiology research. Female athletes remain underrepresented in many exercise physiology studies despite potentially distinct hormonal, inflammatory and

iron-regulatory responses. Menstrual cycle phase, hormonal contraception and relative energy deficiency may significantly influence biomarker interpretation and recovery dynamics.

Emerging literature indicates that psychological resilience and stress tolerance may substantially influence adaptation to prolonged training stress. Consequently, future athlete monitoring systems may increasingly integrate physiological and psychological assessment rather than focusing exclusively on laboratory biomarkers.

Technological progress should complement rather than replace clinical reasoning and individualized athlete management. Even advanced monitoring systems may fail to capture contextual factors such as motivation, emotional stress, sleep quality or competition-related anxiety. Consequently, multidisciplinary interpretation involving physicians, coaches, nutritionists and sports scientists remains essential.

Taken together, future athlete monitoring will probably evolve toward multidimensional individualized systems integrating physiological, biochemical, behavioral and psychological data. Such approaches may ultimately improve recovery optimization, reduce risk of maladaptation and support long-term athlete health and performance sustainability.

Table 3. Proposed Integrated Pathophysiological Model of Non Functional Overreaching

Physiological trigger	Primary response	Secondary consequence	Clinical manifestation
Excessive training load	Increased IL-6	Elevated hepcidin synthesis	Reduced iron availability
Repetitive endurance exercise	Autonomic imbalance	Reduced HRV	Impaired recovery
Sleep restriction	Increased cortisol secretion	Sympathetic predominance	Persistent fatigue
Low energy availability	Endocrine dysregulation	Impaired adaptation	Performance decline
Psychological stress	Increased autonomic strain	Recovery impairment	Mood disturbance
Inadequate regeneration	Chronic physiological stress	Multisystem maladaptation	Non-functional overreaching

Table 3. Proposed Integrated Pathophysiological Model of Non-Functional Overreaching Based on Available Evidence [1,3,20,21,24,29,31]

The model above emphasizes that non-functional overreaching should be interpreted as a multifactorial process involving simultaneous interaction between inflammatory signaling, autonomic regulation, iron metabolism and recovery dynamics.

16. Future Directions

Future research should focus on large-scale longitudinal studies capable of integrating autonomic, inflammatory and iron-regulatory biomarkers with objective performance outcomes [3,7,29,31].

One of the major limitations of current literature involves heterogeneity in athlete populations, training protocols and diagnostic definitions of NFOR and OTS. Standardized monitoring protocols are therefore necessary to improve comparability between studies.

Additional investigation is required to determine whether combined biomarker panels can predict maladaptation before clinically significant performance decline develops. Future studies should also evaluate sex-specific responses, since hormonal status and menstrual blood loss may substantially influence iron metabolism and recovery.

The increasing availability of wearable technology may further improve continuous athlete monitoring. Integration of HRV data with sleep tracking, training load metrics and biochemical markers could facilitate development of individualized early-warning systems.

Artificial intelligence-assisted monitoring platforms may eventually allow identification of maladaptive physiological trends before severe dysfunction occurs. Nevertheless, such approaches require rigorous validation and careful ethical consideration regarding athlete privacy and medical data protection [7,9,13].

From a clinical perspective, future athlete monitoring should prioritize individualized longitudinal assessment rather than isolated threshold-based interpretation.

17. Practical Recommendations

Based on current evidence, several practical recommendations may be proposed for endurance athletes and sports medicine clinicians.

First, HRV monitoring should be performed under standardized morning conditions and interpreted longitudinally rather than as isolated measurements [3,34,35].

Second, persistent reductions in HRV accompanied by fatigue, impaired sleep and performance decline should prompt additional recovery evaluation [3,25,31,35].

Third, iron status monitoring should include ferritin, hemoglobin and transferrin saturation, particularly in athletes exposed to high training volumes [18,19,22,24].

Fourth, hepcidin assessment may provide additional mechanistic insight in selected athletes experiencing recurrent fatigue or unexplained performance decline [20,21,24].

Fifth, training load management should integrate both subjective and objective recovery markers [31,32,33].

Sixth, nutritional strategies aimed at optimizing energy availability and iron intake should be incorporated into athlete management programs [18,19,22,23].

Finally, clinicians should recognize that no isolated biomarker currently provides sufficient diagnostic specificity for NFOR. The most effective strategy appears to involve integration of physiological, biochemical, performance and subjective monitoring domains [1,3,29,31].

18. Strengths of the Review

This review integrates autonomic, inflammatory and iron-regulatory mechanisms involved in non functional overreaching within a single conceptual framework.

Unlike many previous reviews focusing exclusively on HRV or isolated biochemical markers, the present article emphasizes the interaction between autonomic dysregulation, inflammatory activation and iron metabolism disturbances.

Another strength involves the practical sports medicine perspective. The review discusses not only pathophysiological mechanisms but also potential real-world applications in athlete monitoring and recovery assessment.

Additionally, the article highlights the importance of individualized longitudinal monitoring rather than isolated laboratory interpretation.

19. Clinical Perspective

From a practical sports medicine perspective, early recognition of maladaptation remains essential for prevention of long-term performance decline and athlete health deterioration.

The integration of wearable-derived physiological monitoring with laboratory biomarkers may improve individualized athlete management and allow earlier intervention before progression toward overtraining syndrome [3,7,13,31].

Clinicians, coaches and sports scientists should recognize that recovery status cannot be adequately evaluated using a single physiological parameter. Instead, interpretation should involve longitudinal analysis of multiple interacting domains.

20. Practical Clinical Implications

From a practical standpoint, the present review supports implementation of multidimensional athlete monitoring strategies rather than reliance on isolated laboratory parameters. Daily HRV assessment, periodic evaluation of iron status and careful analysis of subjective recovery may together improve recognition of maladaptive physiological trends before clinically significant underperformance develops.

The interaction between inflammatory signaling, autonomic regulation and iron metabolism appears particularly important in endurance athletes exposed to prolonged high-volume training. Consequently, clinicians should consider broader physiological context when interpreting alterations in HRV, inflammatory markers or ferritin concentration.

Importantly, effective prevention of non-functional overreaching requires collaboration between physicians, coaches, nutritionists and sports scientists. Recovery optimization should include individualized training prescription, nutritional support, sleep management and psychological stress reduction.

21. Final Conclusions

Non-functional overreaching represents a multifactorial maladaptive state resulting from imbalance between training load and recovery. Early diagnosis remains challenging because physiological fatigue and pathological maladaptation frequently overlap.

Current evidence suggests that heart rate variability, inflammatory markers and hepcidin each provide clinically relevant information regarding athlete recovery and physiological stress. However, isolated interpretation of these biomarkers demonstrates limited diagnostic specificity.

An integrated monitoring model combining autonomic regulation, inflammatory response, iron metabolism, performance metrics and subjective recovery appears to represent the most clinically meaningful strategy for early detection of maladaptation.

Heart rate variability remains the most practical non-invasive monitoring tool currently available, whereas hepcidin provides mechanistic insight into exercise-induced disturbances in iron regulation. Inflammatory biomarkers may further contribute to understanding cumulative physiological stress.

Future prospective studies are required to determine whether multimodal biomarker panels can reliably predict non-functional overreaching and improve athlete management.

The integration of physiological, biochemical and performance-based monitoring may ultimately improve recovery optimization, reduce risk of overtraining syndrome and support long-term athlete health and performance.

Overall, currently available evidence supports the concept that multidimensional longitudinal monitoring strategies provide substantially greater clinical and practical value than isolated interpretation of single biomarkers. Future research integrating wearable technologies, molecular biomarkers and individualized physiological profiling may further improve prevention and early recognition of maladaptive training responses in endurance athletes [7,9,13].

DISCLOSURE

Supplementary Materials: Not Applicable

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All of the authors read and agreed with the final version of the manuscript.

Funding: This article does not receive any funding
Institutional Review Board Statement: Not Applicable
Informed Consent Statement: Not Applicable
Data Availability Statement: Not Applicable
Acknowledgements: Not Applicable
Conflicts of Interest: The authors declare no conflict of interest in relation to this study
Declaration of generative AI and AI-assisted technologies in the writing process:
In preparing this work, the authors used Claude (Anthropic) for the purpose of language editing and improving the readability of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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