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REVIEW ARTICLE

Assessing Overtraining Syndrome in Competitive Athletes: Biomarkers, Screening Tools, and Clinical Correlates

a narrative review

HIGHLIGHTS

- OTS is a multifactorial syndrome combining hormonal, immune, autonomic and metabolic dysregulation; up to 64% of male and 60% of female athletes are affected.
- No single biomarker is pathognomonic — the EROS programme identified 45+ candidate markers, none universally diagnostic in isolation.
- The testosterone/cortisol (T/C) ratio, pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), leptin and urinary catecholamines are the most informative biomarker families.

- Multidomain monitoring — physiological, psychological, performance and load metrics — outperforms any single parameter for early detection.
- Prevention rests on integrated load–recovery monitoring, sleep, nutrition and psychological support; emerging tools include wearables and fMRI of central fatigue.

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ABSTRACT

BACKGROUND: Overtraining syndrome (OTS) is a multifactorial clinical condition resulting from an imbalance between training load and recovery. It affects up to 64% of male and 60% of female athletes at least once during their career and carries significant consequences for physical performance, hormonal balance, immune function, and mental health. Despite its prevalence, OTS remains poorly defined and difficult to diagnose due to the absence of a single validated biomarker and substantial overlap with other conditions common in athletic populations.

AIM: To review the current evidence on the pathophysiology, diagnostic approaches, biomarkers, and prevention strategies related to overtraining syndrome, and to evaluate the utility of existing and emerging diagnostic frameworks.

MATERIALS AND METHODS: A thorough analysis was conducted following PRISMA recommendations. Research data were derived from the scientific databases Embase, PubMed and Google Scholar. Keywords were selected based on their relevance to the review subject.

RESULTS: OTS arises from the interaction of metabolic, immunological, neuroendocrine, and autonomic dysregulation. The EROS study identified over 45 candidate biomarkers, yet none proved universally diagnostic. Multidomain assessment combining hormonal, immunological, and autonomic markers demonstrated superior diagnostic value over any single parameter. Prevention relies on integrated monitoring of training load, recovery, nutrition, sleep, and psychological well-being.

CONCLUSIONS: OTS diagnosis requires comprehensive clinical evaluation and systematic exclusion of alternative aetiologies. No pathognomonic marker exists; therefore, multiparametric frameworks remain the most reliable diagnostic approach. Early detection and prevention through multidimensional athlete monitoring constitute the most effective clinical strategy.

KEYWORDS overtraining syndrome; athletes; biomarkers; screening; fatigue; recovery; EROS study

GRAPHICAL ABSTRACT

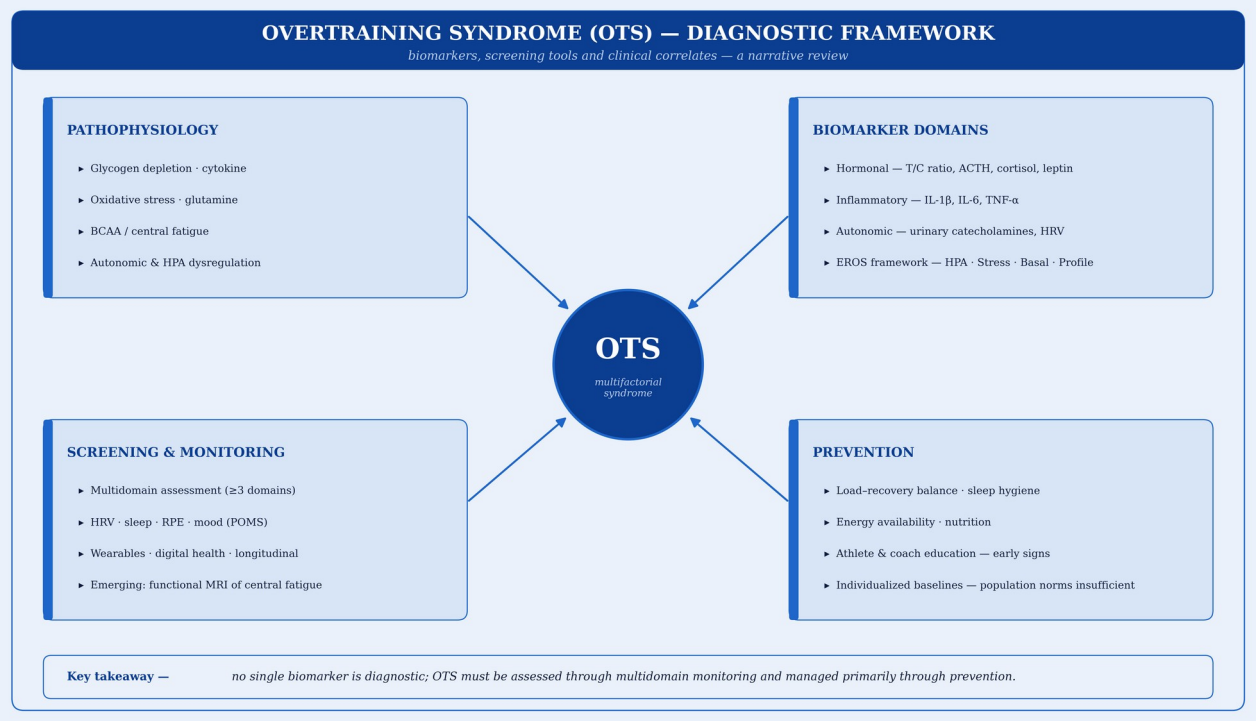

Figure 1. *Conceptual overview of overtraining syndrome — pathophysiology, biomarker domains (hormonal, inflammatory, autonomic and the EROS framework), screening and monitoring strategies, and prevention pillars discussed in this narrative review.*

PLAIN LANGUAGE SUMMARY

Overtraining syndrome (OTS) is a state in which an athlete trains hard but, instead of getting fitter, gets persistently tired, performs worse, and may experience mood, sleep and immune problems that last for months. It occurs when the balance between training stress and recovery breaks down. Although very common — up to two thirds of athletes experience it at least once — OTS is hard to

diagnose because there is no single blood test that confirms it. Researchers from the EROS programme tested dozens of candidate biomarkers and found that combinations of hormones (cortisol, testosterone, the T/C ratio), inflammatory signals (TNF-α, IL-6, IL-1β), adipokines such as leptin, and urinary catecholamines provide the most useful clues. New tools — wearable sensors, heart-rate variability, sleep tracking and even functional brain imaging — may detect overtraining earlier. The strongest message of this review is that prevention is more effective than diagnosis after the fact: athletes need carefully planned training loads, enough rest, good nutrition and psychological support, and coaches need to take early warning signs such as persistent fatigue and mood changes seriously.

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1. INTRODUCTION

Regular, well-structured physical training is widely recognized as a fundamental component of improving athletic performance and overall health. When appropriately dosed, exercise induces beneficial

physiological adaptations, including enhanced muscular strength, endurance, and sport-specific capabilities. These benefits are contingent upon a balance between training load and recovery. When this balance is disrupted — particularly in the context of high-intensity or high-volume training — adaptive processes may give way to maladaptive responses. Athletes, especially at elite levels, are frequently exposed to substantial physical and psychological demands, often accepting fatigue, minor injuries, and mental strain as inherent aspects of performance development. Yet, excessive training without adequate recovery can lead to a progressive decline in performance and well-being (Shorter et al., 2026).

Understanding overtraining syndrome (OTS) is significant for both competitive and recreational athletes as many people exceed their physical limits without proper awareness. It impacts not only physical performance but also hormonal balance, immune function, and mental health (Fiala et al., 2025).

2. OVERTRAINING SYNDROME — DEFINITION AND BIOMARKERS

2.1 Overtraining Syndrome — Definition and Differentiation

Overtraining syndrome (OTS) is a multifactorial clinical condition observed in individuals exposed to sustained high physical and psychological demands. It is best conceptualized along a continuum of well-being, in which an individual's functional state shifts in response to the dynamic interaction between training-related stress (load) and recovery. This continuum extends from physiological homeostasis through adaptive responses to progressively maladaptive states that may culminate in injury, illness, or severe systemic dysfunction.

Training load comprises a broad range of stressors, including physiological, mechanical, and psychological factors originating both within and beyond the sporting context. It is distinguished into external load — objective demands such as training intensity, volume, frequency, and life-related stressors — and internal load, which reflects the individual's biological and psychological responses to these demands. Internal load can be assessed using both objective and subjective measures.

Recovery works in the opposite direction, facilitating restoration of homeostasis through adequate rest, nutrition, hydration, and psychological regeneration. The balance between load and recovery is therefore critical in determining adaptation versus maladaptation (Haghighat and Stull, 2024).

Responses to excessive training load exist along a spectrum defined by the magnitude and duration of performance impairment, categorized as functional overreaching (FOR), non-functional overreaching (NFOR), and overtraining syndrome (OTS). FOR represents a transient state in which short-term performance reduction is followed by supercompensation and subsequent performance enhancement. NFOR is characterized by stagnation or continued decline in performance, commonly accompanied by fatigue and emotional dysregulation notwithstanding days of recovery time. FOR and NFOR can usually be reversed with variable rest periods lasting weeks or months. When maladaptive responses persist longer than 2 months, along with sustained fatigue, psychological symptoms, and evidence of systemic dysregulation, the condition may progress to OTS (Shorter et al., 2026).

Overtraining syndrome is defined by a persistent reduction in athletic performance that does not resolve despite appropriate periods of rest. It is commonly associated with a constellation of symptoms, including excessive fatigue, prolonged muscle soreness, impaired sleep quality, decreased motivation,

mood disturbances, and a subjective sense of exhaustion or "staleness". The development of OTS is multifactorial, with contributing factors such as insufficient nutritional intake, inadequate sleep, and elevated psychological stress. In particular, deficits in calories, protein and carbohydrate availability have been identified as key contributors.

Up to 64% of male and 60% of female athletes experience OTS at least once during their career, and it is less common in team sports than in individual sports (Buchwald et al., 2025). Athletes with a prior history of OTS appear to have a substantially increased risk of recurrence. Although some investigations have described even higher prevalence rates of OTS and related conditions, these figures may be inflated due to inconsistent and overlapping definitions of FOR, NFOR, and OTS. At present, no definitive epidemiological data exist along with strict diagnostic criteria (Haghighat and Stull, 2024; Buchwald et al., 2025).

2.2 Pathophysiological Hypotheses of OTS

The pathophysiology of OTS is complex and likely multifactorial, with no single mechanism fully explaining its development. Instead, several interrelated hypotheses have been proposed. Although these models provide valuable insights, none alone accounts for the full clinical picture, suggesting that OTS emerges from the interaction of metabolic, immunological, neuroendocrine, and biochemical processes.

Glycogen depletion hypothesis — repeated high-intensity exercise with inadequate carbohydrate replenishment leads to chronically reduced muscle glycogen stores, impairing energy availability and promoting fatigue. Prolonged depletion may also shift metabolism toward increased amino acid oxidation. It does not fully explain OTS, as symptoms may also occur in athletes maintaining adequate carbohydrate intake and normal glycogen levels.

Cytokine hypothesis — excessive training loads lead to cumulative damage in muscles, tendons, and joints, activating immune responses and promoting the release of pro-inflammatory cytokines: IL-1β, IL-6 and TNF-α. These mediators influence not only local tissue repair but also immune and CNS activity, endocrine function, and energy metabolism. They may contribute to fatigue, mood alterations, reduced appetite, and impaired recovery, thereby linking peripheral inflammation with central symptoms characteristic of OTS.

Oxidative stress hypothesis — assumes an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant systems, leading to cumulative cellular damage and reduced functional capacity. Intensive and prolonged exercise markedly increases oxygen consumption, thereby enhancing ROS generation. While moderate oxidative stress plays a role in physiological adaptation, excessive accumulation of reactive species can damage lipids, proteins, and nucleic acids, disrupt mitochondrial function, and exacerbate inflammatory pathways.

Glutamine hypothesis — glutamine is a key amino acid for immune cell metabolism and nitrogen transport. Sustained high loads may increase its utilization and reduce circulating levels, particularly when recovery periods are insufficient. This reduction could impair immune competence, increasing susceptibility to infections frequently observed in overtrained individuals.

Central fatigue and branched-chain amino acid hypothesis — during prolonged exercise, increased oxidation of BCAAs reduces their plasma concentration, thereby decreasing competition with tryptophan

for transport across the blood–brain barrier. Enhanced tryptophan availability promotes serotonin synthesis, which has been associated with increased perceptions of fatigue, altered sleep patterns, and mood disturbances.

Autonomic and hypothalamic hypothesis — dysregulation of the autonomic nervous system, characterized by reduced sympathetic activity and relative parasympathetic dominance, may contribute to fatigue, decreased performance, and bradycardia. An initial phase of heightened sympathetic activation can precede this state, followed by exhaustion with diminished catecholamine release or responsiveness. Concurrently, alterations in hypothalamic–pituitary axes have been proposed, with blunted hormonal responses to stress and exercise (e.g., ACTH, cortisol, and gonadal hormones). However, findings remain inconsistent, suggesting significant individual variability and limiting definitive conclusions (Brel et al., 2023; Fiala et al., 2025).

2.3 Biomarkers in the Diagnosis of OTS — the EROS Study

In order to standardize the diagnosis of OTS, an attempt was undertaken to establish diagnostic criteria; however, it should be emphasized that rigid guidelines have not been defined. Current diagnostic practice is informed by the Endocrine and Metabolic Responses on Overtraining Syndrome (EROS) study (Cadegiani et al., 2020). This landmark investigation was conducted by Flavio Cadegiani and Claudio Kater in 2019. Its objective was to facilitate the diagnosis of OTS and to provide a clearer definition and understanding of the condition. The study included 51 participants, divided into athletes with OTS (n=14), healthy athletes (n=25), and healthy physically inactive individuals as controls (n=12). The authors analysed 67 parameters, among which more than 45 biomarkers potentially useful in the diagnosis of OTS were identified. On this basis different variants of the EROS system were distinguished, such as EROS-HPA, EROS-stress, EROS-basal and EROS-profile — briefly described in Table 1 (Fiala et al., 2025). Among the biomarkers facilitating diagnosis there are hormonal, immunological and autonomic markers. Of the 67 parameters, 23 remained unchanged across all three studied groups; however, none of the evaluated markers was present in all athletes affected by OTS. This indicates that no single unique marker was identified whose presence in an athlete could unequivocally confirm the occurrence of OTS. Each examined individual demonstrated a specific composition of biomarkers and parameters that may indicate OTS. Therefore, the identification of combinations of biomarkers proved more reliable and accurate for assessment and diagnosis than the analysis of any single parameter.

EROS subcategory	Description	Representative examples
EROS-HPA	Assessment of hypothalamic–pituitary–adrenal (HPA) axis function through hormonal responses to stress or exercise stimuli.	Cortisol response to an exercise test; ACTH response following stimulation.
EROS-STRESS	Response of the organism to physical or psychological stress, particularly adaptive and	Cortisol changes after stress; heart-rate variability (HRV) in

	recovery capacity.	response to stress.
EROS-BASAL	Resting basal measurements performed without additional stimulation, reflecting the baseline state of the organism.	Morning cortisol; resting testosterone.
EROS-PROFILE	Comprehensive interpretation of hormonal, immunological and autonomic results, forming an individual physiological profile of the athlete.	Integrated analysis of blood results and responses to exercise.

Table 1. *EROS subcategories — definitions and representative examples (adapted from Cadegiani & Kater, 2019a).*

2.4 Testosterone/Cortisol Ratio

One of the important hormonal biomarkers of OTS is the testosterone/cortisol (T/C) ratio. Testosterone is an anabolic hormone, cortisol a catabolic one. Their ratio may assist in determining the intensity of anabolic versus catabolic processes occurring in the organism and which of them is predominant. A decreased T/C ratio could indicate the dominance of catabolic metabolism and the predominance of tissue breakdown over tissue synthesis, manifested by chronic fatigue and constituting one of the components of OTS. However, reliance on this single marker presents diagnostic challenges, because a decreased T/C ratio is not always unequivocally associated with OTS and may result from various other causes, such as an isolated decrease in testosterone levels or an increase in cortisol levels. As with other indicators discussed in the EROS study, the T/C ratio should not be considered independently, but in relation to the patient's clinical condition, symptoms and other indicators (Nowicka et al., 2026).

2.5 Immunological Markers — Cytokines

Physical exercise may stimulate both pro- and anti-inflammatory responses (Cerqueira et al., 2020). Overtraining leads to oxidative stress and increased secretion of inflammatory markers — pro-inflammatory cytokines. Excessive training leads to an increase in the secretion of pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6 (Docherty et al., 2022). It has been shown that under optimal training and recovery conditions TNF-α levels decrease, whereas in overtraining they increase. This and other pro-inflammatory cytokines contribute to the pathogenesis of OTS, as they mediate the inflammatory response that occurs during muscle damage from excessive training. Pro-inflammatory cytokines, particularly TNF-α, mediate the majority of symptoms associated with OTS, including reduced endurance, sleep disturbances, stress, impaired immune response and frequent upper respiratory tract infections.

2.6 Adipokines

In response to physical exertion, adipose tissue undergoes remodelling and produces adipokines — cytokines of adipose origin that act as mediators of numerous processes occurring in the organism (Mika et al., 2019). Extensive physical exercise promotes a pro-inflammatory state in adipose tissue. One of the pro-inflammatory adipokines produced by adipose tissue is leptin. However, as demonstrated by Luti et al. (2020), in overtrained individuals exhibiting symptoms of OTS, leptin levels decrease. This effect is particularly pronounced following prolonged physical exertion and under conditions of chronic training,

which result in metabolic changes such as adipose tissue remodelling. Despite its pro-inflammatory activity, leptin plays a significant role in maintaining hormonal balance and regulating long-term energy balance. Prolonged intensive physical exertion and insufficient recovery may lead to hormonal and metabolic disturbances, including decreased leptin levels, which is associated with reduced performance and the risk of developing OTS.

2.7 Urinary Catecholamines

Catecholamines, which include dopamine, adrenaline and noradrenaline, are molecules produced in the adrenal medulla that function both as neurotransmitters and hormones essential for maintaining homeostasis through the autonomic nervous system. During intensive physical exertion the level of catecholamines excreted in urine changes; therefore, they may constitute a useful biomarker supporting the diagnosis of OTS (Casadio, 2021), one that is also convenient to obtain in a non-invasive manner. Lower concentrations of noradrenaline in plasma observed during maximal exertion have been attributed in some studies to adrenal fatigue. An association has been demonstrated (Mackinnon et al., 1997) between OTS and the presence of catecholamines in urine in elite swimmers — low urinary excretion of noradrenaline was observed 2–4 weeks prior to the onset of OTS symptoms, an effect attributed to reduced adrenal function resulting from excessive physical exertion.

3. DISCUSSION AND FUTURE PERSPECTIVES

3.1 Discussion

Despite considerable advances in exercise physiology and sports medicine, the diagnosis of OTS remains a significant clinical and scientific challenge. The condition relies on multifactorial evaluation of both subjective and objective indicators rather than a single definitive diagnostic test. Clinicians typically assess an athlete's symptoms, training history, and performance changes, often supplemented with psychometric questionnaires and physiological biomarkers such as hormonal or inflammatory markers (Madzar et al., 2023). However, these approaches lack standardized diagnostic criteria and sufficient validation against gold-standard methods, and OTS is predominantly diagnosed retrospectively, following sustained performance decrements that may persist for weeks or months — substantially limiting opportunities for early clinical intervention (Meur et al., 2014).

A fundamental diagnostic obstacle is the lack of operationalized thresholds that systematically distinguish FOR, NFOR, and OTS along a pathophysiological continuum (Madzar et al., 2023). Although transient reductions in performance and heightened fatigue are anticipated responses to increased training stimuli, OTS is conventionally characterized by a prolonged performance decrement persisting despite adequate recovery (Armstrong et al., 2022). However, this distinction remains largely descriptive rather than defined through measurable, reproducible clinical criteria. Considerable heterogeneity exists across studies with respect to the duration and severity of symptoms required for diagnosis, limiting cross-study comparability and reducing the reliability of epidemiological estimates (Meur et al., 2014; Costa et al., 2022).

The absence of a single validated biomarker constitutes another critical diagnostic limitation. A broad range of physiological, hormonal, immunological, and metabolic parameters — including cortisol,

testosterone, catecholamines, inflammatory cytokines, and markers of oxidative stress — have been proposed as potential indicators of OTS (Cadegiani & Kater, 2019a; Carrard et al., 2021). Nevertheless, these parameters exhibit substantial inter-individual variability and are susceptible to confounding influences including circadian rhythmicity, nutritional status, psychological stress, and cumulative training history. None has demonstrated adequate diagnostic sensitivity or specificity when evaluated in isolation (Fiala et al., 2025). This highlights the need for more reliable and objective measures capable of differentiating OTS from conditions with overlapping clinical presentations.

Research conducted within the framework of the EROS project has advanced understanding of the complex physiological alterations associated with OTS. These investigations identified multiple endocrine and metabolic disturbances in affected athletes, including dysregulation of the HPA axis, disruption of anabolic–catabolic hormonal balance, and impaired metabolic adaptation to exercise-induced stress (Cadegiani & Kater, 2019a). Critically, however, these findings reinforce the multifactorial pathophysiology of the syndrome. Rather than delineating a single diagnostic marker, the EROS studies suggest that OTS reflects systemic dysregulation across multiple physiological pathways, further complicating the development of straightforward diagnostic tests. Complementary findings from the EROS-DISRUPTORS study indicate that non-training stressors — including insufficient caloric intake, poor sleep quality, and psychosocial burden — contribute substantially to syndrome development (Cadegiani & Kater, 2019b). These data support the conceptualization of OTS as the cumulative consequence of multiple intersecting stressors rather than a product of excessive training volume alone, with important implications for both diagnosis and clinical management.

The clinical presentation of OTS is further complicated by the nonspecific nature of its symptomatology. Affected athletes commonly report persistent fatigue, reduced training tolerance, mood disturbances, sleep disruption, and diminished motivation, manifestations which are not pathognomonic for OTS and may arise in a range of conditions prevalent in athletic populations, including infectious illness, iron deficiency anaemia, endocrine disorders, and relative energy deficiency in sport (RED-S) (Armstrong et al., 2022; Chernozub et al., 2024). Accordingly, clinicians must undertake systematic differential diagnostic evaluations prior to attributing performance decrements to OTS. Psychological symptomatology represents a similarly important yet diagnostically challenging dimension. Mood disturbances, irritability, and heightened perceived stress have been consistently documented in athletes experiencing maladaptation to training loads, and validated instruments such as the Profile of Mood States (POMS) have been proposed as screening tools (Costa et al., 2022). However, their subjective nature and susceptibility to confounding from non-training-related stressors — including academic, social, and personal life factors — limit their diagnostic utility as standalone measures (Madzar et al., 2023).

3.2 Emerging Diagnostic Approaches

In parallel with established peripheral biomarker assessment, monitoring of hematological and biochemical markers during periods of intensified training may help identify early signs of functional overreaching before progression to OTS. A study by Clemente et al. (2021) examining professional soccer players during preseason training reported increases in platelet counts alongside reductions in absolute neutrophil and monocyte counts and calcium levels, as well as significant elevations in creatinine, alkaline phosphatase, C-reactive protein, cortisol, and testosterone following preseason training loads. Systematic

tracking of such hematological and biochemical changes may offer insight into athletes' physiological responses to fluctuating training demands and could contribute to the early detection of maladaptive stress responses prior to overt clinical manifestation.

Recent neuroimaging research offers a further promising mechanistic perspective. Functional magnetic resonance imaging (fMRI) has been proposed as a novel screening approach targeting central nervous system correlates of OTS (Blain et al., 2019). Unlike peripheral biomarkers such as hormones or cytokines, neuroimaging captures the central fatigue component of the syndrome and may reveal neural signatures associated with maladaptive responses to training stress. Nevertheless, fMRI currently remains a research tool rather than a validated clinical diagnostic instrument, and imaging cannot at present directly diagnose OTS (Madzar et al., 2023). It may, however, play an important ancillary role in evaluating secondary complications associated with overtraining, including bone stress injuries. The identification of reproducible neural patterns associated with excessive training load may eventually contribute to future diagnostic frameworks, particularly when integrated with biochemical and physiological markers within a multidomain assessment model (Fiala et al., 2025).

3.3 Prevention and Monitoring

Given these diagnostic constraints, increasing research attention has been directed toward multidimensional monitoring strategies capable of detecting early signs of maladaptation prior to the development of overt OTS (Madzar et al., 2023). Current evidence supports the integration of physiological, psychological, and performance-based indicators into comprehensive athlete monitoring systems, acknowledging that meaningful diagnostic signals are more likely to emerge from the convergence of multiple measures than from any single variable in isolation (Fiala et al., 2025).

Monitoring of training load and recovery balance remains among the most widely recommended preventive approaches. Objective physiological indicators including heart rate variability, resting heart rate, training volume, and performance metrics provide valuable information regarding physiological stress and recovery status (Costa et al., 2022). Complementarily, subjective assessments such as ratings of perceived exertion, fatigue scales, sleep quality questionnaires, and mood inventories may capture early perturbations in athlete well-being that precede detectable physiological alterations (Fiala et al., 2025). Systematic integration of these data streams into athlete management platforms enables coaches and sports medicine practitioners to identify deviations from an athlete's individual baseline and implement timely training load modifications (Chernozub et al., 2024).

Advances in wearable sensor technologies and digital health platforms offer additional promise for the continuous, ecologically valid monitoring of physiological parameters including heart rate variability, sleep architecture, and daily training load (Fiala et al., 2025). When combined with structured subjective wellness reporting and performance monitoring, these tools may facilitate earlier detection of physiological stress signatures that are difficult to capture through periodic clinical assessment alone (Armstrong et al., 2022). However, the substantial inter-individual physiological variability inherent to athletic populations necessitates careful individualized interpretation of such data, and standardized protocols for clinical application remain to be established (Chernozub et al., 2024).

Preventive frameworks must also systematically address non-training stressors that contribute to total physiological load. Maintenance of adequate energy availability is essential to support metabolic recovery and preserve endocrine homeostasis, and insufficient caloric intake has been implicated as a contributing factor in athletes presenting with OTS-consistent symptomatology (Cadegiani & Kater, 2019a; Chernozub et al., 2024). Sleep quality and psychological recovery represent equally critical components; chronic sleep restriction impairs physiological recuperation and may potentiate the adverse effects of intensive training, while psychosocial stressors unrelated to sport may interact with training-induced physiological load to heighten maladaptation risk (Armstrong et al., 2022). Effective prevention therefore necessitates holistic recovery strategies encompassing nutritional adequacy, sleep hygiene optimization, and psychological well-being support (Costa et al., 2022).

Education of athletes, coaches, and multidisciplinary support staff constitutes a further essential preventive pillar. Timely recognition of early warning signs including persistent fatigue, prolonged muscular soreness, irritability, motivational decline, and unexplained performance deterioration can facilitate prompt training program modification before chronic maladaptation is established (Engler et al., 2026). Clear and open communication channels between athletes and medical personnel are particularly important, as competitive pressures may lead athletes to conceal emerging symptoms, delaying clinical recognition (Chernozub et al., 2024).

3.4 Future Directions

Notwithstanding these advances, substantial gaps persist in the current understanding of OTS. Future research should prioritize prospective longitudinal cohort studies tracking athletes across complete training cycles while systematically integrating physiological, psychological, and environmental data. The development of integrated diagnostic frameworks such as the EROS diagnostic model — which incorporates clinical symptomatology, biochemical profiling, and hormonal stimulation testing into a structured protocol (Carrard et al., 2021) — represents an important step toward standardization, though further validation across diverse athletic populations and sporting disciplines is required. Of particular importance is the validation of multidomain diagnostic models that combine physiological monitoring, biochemical markers, and emerging tools such as neuroimaging to improve the accuracy and reliability of OTS identification and its differentiation from other fatigue-related conditions (Engler et al., 2026). Advances in wearable technologies, big-data analytics, and machine learning may further support the identification of predictive patterns of physiological maladaptation and the development of individualized, adaptive training prescriptions (Fiala et al., 2025).

4. CONCLUSIONS

Overtraining syndrome represents a complex, multifactorial clinical condition that continues to pose substantial challenges across diagnostic, epidemiological, and management domains. The absence of a single pathognomonic biomarker, combined with the nonspecific and heterogeneous nature of its clinical presentation, means that diagnosis remains an exercise in systematic exclusion and multiparametric evaluation rather than confirmation through any one definitive test. The overlapping continuum from functional overreaching through nonfunctional overreaching to fully established OTS further complicates

clinical differentiation and limits the reliability of prevalence estimates derived from the existing literature.

The pathophysiological mechanisms underlying OTS are likely to be inherently interrelated rather than operating in isolation. The glycogen depletion, cytokine, oxidative stress, central fatigue, and autonomic dysregulation hypotheses each illuminate important facets of the syndrome; however, none alone adequately accounts for its full clinical expression. This mechanistic complexity is reflected in the findings of the EROS studies, which identified systemic dysregulation across multiple hormonal, immunological, and autonomic pathways in affected athletes, while simultaneously highlighting the degree of inter-individual variability that renders universal diagnostic thresholds elusive. The recognition that non-training stressors — including caloric insufficiency, sleep disruption, and psychosocial burden — contribute substantially to total physiological load underscores the need to conceptualize OTS as a condition arising from cumulative multidomain stress rather than excessive physical training volume alone.

Given these diagnostic and pathophysiological complexities, prevention and early detection must be regarded as the primary clinical priorities. Multidimensional monitoring frameworks that integrate objective physiological parameters, validated subjective wellness instruments, and emerging technologies such as wearable sensors and digital health platforms offer the most promising means of identifying athletes at elevated maladaptation risk before frank OTS is established. Importantly, such monitoring must be individualized, as population-level reference ranges are insufficient to capture the physiological variability characteristic of trained athletic cohorts.

Meaningful progress in the clinical management of OTS will require coordinated efforts spanning standardization of diagnostic criteria, development of longitudinal evidence, and integration of multidomain monitoring strategies. Until pathognomonic markers are identified and validated, a comprehensive clinical approach remains the most defensible framework for both diagnosis and prevention of this challenging syndrome.

5. DISCLOSURE

5.1. Author Contributions

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Data sharing is not applicable to this article as no new data were created or analysed.

5.7. Acknowledgements

None.

5.8. Declaration of Generative AI Use

During the preparation of this work, the authors used Google's Chat Generative Pre-trained Transformer (Gemini 3) to support the editing process, including grammar, spelling, punctuation, and stylistic refinement. All content generated with AI assistance was carefully reviewed and revised by the authors, who accept full responsibility for the accuracy, interpretation, and integrity of the final manuscript.

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