FROM METABOLIC STRESS TO OPTIMAL PERFORMANCE: THE ROLE OF BIOMARKERS IN MONITORING SPORTS OVERTRAINING

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Abstract

Introduction: Sports overtraining represents a complex neuro-endocrino-metabolic condition that develops when the balance between training stress and the body's recovery capacity is persistently disrupted. In this state, marked alterations in biochemical homeostasis occur, including disturbances in energy metabolism, increased catabolic processes, and imbalance in the hypothalamic–pituitary–adrenal (HPA) axis. At the cellular and molecular level, overtraining is associated with increased markers of muscle damage such as creatine kinase (CK), elevated cortisol as a response to physiological stress, and reduced anabolic hormones such as testosterone, reflecting a shift toward a catabolic state. In parallel, activation of systemic inflammatory processes is observed, reflected among others by an increase in C-reactive protein (CRP), an important marker of acute and chronic inflammation related to prolonged physical stress. Additionally, changes in oxidative processes may be observed, contributing to chronic fatigue and reduced adaptive capacity of the organism. In this context, biochemical biomarkers represent objective and measurable tools for assessing the athlete's physiological status, enabling early identification of metabolic imbalances before they become clinically evident. The integration of these laboratory parameters with functional performance assessment provides a more accurate approach to monitoring training load and preventing overtraining.
Aim: This study aims to evaluate the role of creatine kinase (CK), cortisol, testosterone, and CRP in monitoring metabolic stress and preventing overtraining in active athletes.
Materials and Methods: The study included 30 patients (15 active athletes and 15 non-athletes). Anamnestic data were collected (BMI, training frequency, injury history, sleep quality, and fatigue). Laboratory analyses were performed for CK, cortisol, testosterone, and CRP, and the testosterone/cortisol ratio (T/C) was evaluated. Biochemical analyses (CK, cortisol, CRP) were conducted using the Selectra Mach 5, based on enzymatic and spectrophotometric methods. Testosterone was determined using the YHLO iFlash 1200, employing the CLIA method. Samples consisted of serum obtained from venous blood, and analyses were performed with internal quality control. The T/C ratio was calculated from the obtained values.
Results: It is expected that athletes with high training load will show increased CK, cortisol, and CRP levels, decreased testosterone, and a reduced T/C ratio, accompanied by decreased performance and increased subjective fatigue.
Conclusion: Biochemical biomarkers represent valuable tools for monitoring physiological stress and may contribute to the prevention of overtraining and the optimization of sports performance.

Keywords: performance, metabolic stress, hormonal stress, burnout, testosterone, cortisol, CRP.

Introduction

Sports performance and athlete monitoring have undergone remarkable advancements in recent years, driven by the integration of cutting edge scientific approaches (Seshadri, D.R.; et al., 2026). Traditionally, coaches and sports scientists relied on subjective measures to assess an athlete's condition, which often led to a lack of precision and limited understanding of the underlying physiological responses. However, with the advent of biomarker research, the landscape of sports science has been revolutionized, offering objective and quantifiable insights into an athlete's biological state (Lee, E.C.; et al., 2026).

Biomarkers have emerged as powerful tools in elite sports, offering valuable in sights into athletes physiological responses and potential performance enhancement (Pedlar, C.R.; et al, 2026). This discussion explores the significance and potential applications of biomarkers in optimizing elite sports performance, emphasizing their crucial role in supporting athletes' training, recovery, and overall success. Biomarkers provide objective measures of an athlete's physiological state, going beyond traditional subjective performance assessments (Lee, E.C.; et al., 2026). Coaches and sports scientists can utilize blood and salivary biomarker analysis to gain precise data on an athlete's readiness and recovery status, making evidence-based decisions to optimize athletic performance (Haller, N.;et al, 2026). Biomarker analysis enables coaches to tailor training and recovery strategies based on athletes specific biomarker profiles, maximizing training adaptations, minimizing injury risks, and fostering peak performance (McFadden, B.A.;et al, 2026). The intensive training regimens in elite sports can lead to overtraining and fatigue, potentially affecting an athlete's performance and wellbeing. Biomarker analysis, particularly for markers related to inflammation and muscle damage, allows for early detection of these conditions, prompting appropriate adjustments in training loads and recovery interventions (Haller, N.;et al, 2026). It is a well-known fact that resistance exercise can provide a potent stimulus for acute changes in endocrine responses and inflammatory reactions (Izquierdo M.,et al, 2009), (Kraemer W.J.,et al, 2005).
Resistance exercise is a stress factor that triggers a response from most systems of the human body, such as the cardiovascular, respiratory, immune, endocrine, and musculoskeletal systems (McDougle J.M.,et al, 2023). Mechanisms of homeostatic control include the response of multiple regulators of the endocrine system such as the hypothalamic corticotroph (pituitary) axis and locus caeruleus/norepinephrine system, hormones such as testosterone, prolactin, growth hormone, and the specific response of the cytokine system (Tu H., Li Y.-L., 2023), (Jiang Q.,et al, 2020). The physiological stress caused by intensive resistance exercise acts as a major stimulus for muscle fiber hypertrophy, and efficient muscle repair requires a well-coordinated and controlled inflammatory response (Peake J.M.,et al, 2016). The results of Chycki et al. (2024) indicate that resistance exercise causes a short term increase in testosterone, which returns to baseline within one hour. CK activity also increases after exercise, while CRP remains unchanged. Cortisol responses differ depending on the exercise, decreasing after bench press but not after leg press, suggesting a condition specific effect (Chycki, J.,et al, 2024).

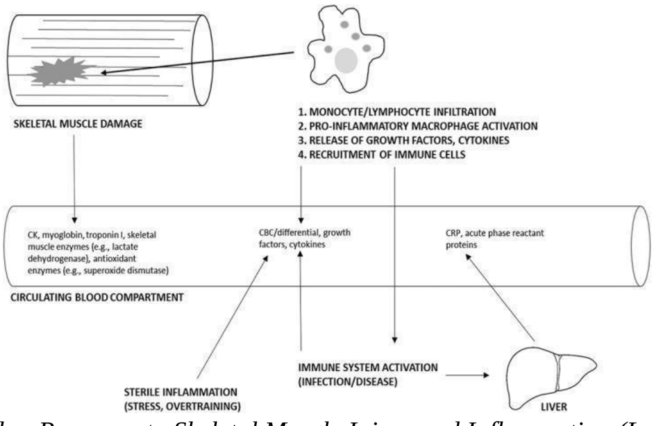


Fig.1: Systemic Biomarker Response to Skeletal Muscle Injury and Inflammation (Lee, E. C., Fragala, M. S., Kavouras, S. A., Queen, R. M., Pryor, J. L., & Casa, D. J. (2017). Biomarkers in Sports and Exercise: Tracking Health, Performance, and Recovery in Athletes. Journal of strength and conditioning research, 31(10), 2920–2937.

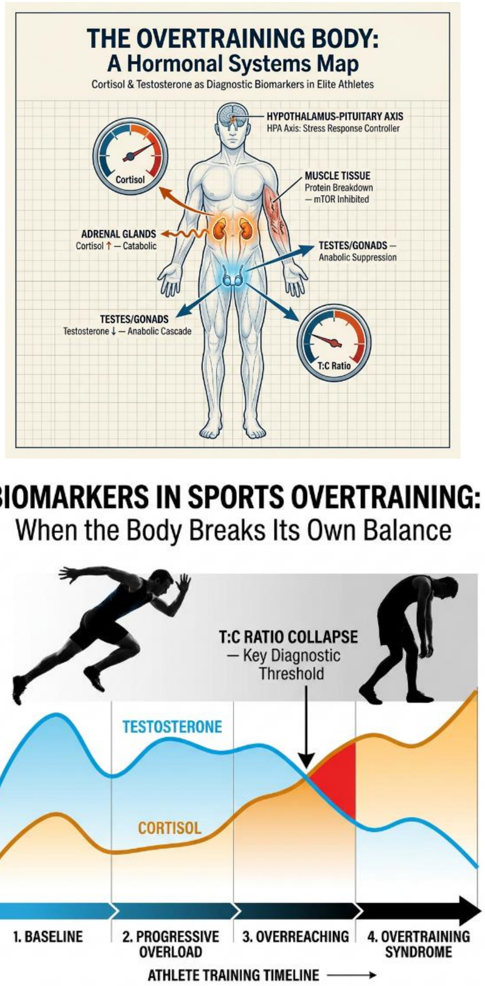


Fig.2: Cortisol–Testosterone imbalance and systemic effects in overtraining syndrome

In sports medicine, creatine kinase (CK), testosterone, cortisol, and C-reactive protein (CRP) are commonly used as interconnected markers to assess the physiological and inflammatory response to exercise and recovery status (Kreher & Schwartz, 2012; Peake et al., 2017). CK is primarily considered an indicator of muscle fiber disruption, with elevated levels reflecting exercise induced muscle damage, particularly after high intensity or unaccustomed resistance training (Peake et al., 2017). Testosterone is an anabolic hormone that supports muscle protein synthesis and recovery, and it often shows an acute post exercise increase, especially following resistance exercise, although this response is typically transient (Urhausen & Kindermann, 2002). Cortisol, a key catabolic stress hormone, rises in response to physiological stress and energy demand, and its balance with testosterone is frequently used to evaluate the anabolic–catabolic state of an athlete (Urhausen & Kindermann, 2002; Kreher & Schwartz, 2012). A higher testosterone-to-cortisol ratio is generally interpreted as a more favorable environment for recovery and adaptation, while a shift toward elevated cortisol may indicate excessive training stress or insufficient recovery (Kreher & Schwartz, 2012). CRP, on the other hand, is a systemic inflammatory marker that tends to increase in response to more substantial or prolonged tissue stress, although it may remain unchanged after moderate or well tolerated exercise bouts (Kasapis & Thompson, 2005; Peake et al., 2017). Together, these biomarkers provide complementary information: CK reflects structural muscle stress, testosterone and cortisol reflect endocrine regulation of adaptation and stress, and CRP reflects systemic inflammation. In combination, they are widely used in sports medicine to monitor training load, detect overreaching, and guide recovery strategies in athletes (Kreher & Schwartz, 2012).

Purpose of the study

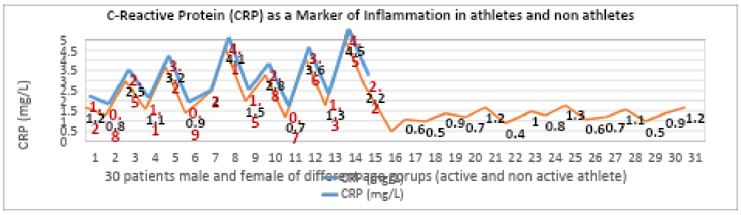
This study aims to evaluate the role of creatine kinase (CK), cortisol, testosterone, and C-reactive protein (CRP) in assessing metabolic stress and their potential utility in monitoring training load and preventing overtraining syndrome in active athletes.

Material and method

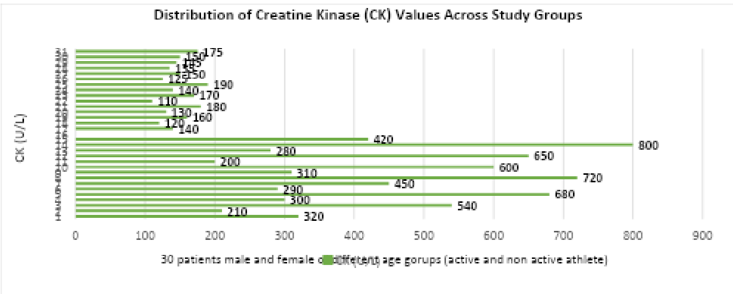
The study included 30 patients (15 active athletes and 15 non-athletes patients from different genders and age groups). Anamnestic data were collected (BMI, training frequency, injury history, sleep quality, and fatigue). Laboratory analyses were performed for CK, cortisol, testosterone, and CRP, and the testosterone/cortisol ratio (T/C) was evaluated.
Biochemical analyses (CK, cortisol, CRP) were conducted using the Selectra Mach 5, based on enzymatic and spectrophotometric methods. Testosterone was determined using the YHLO iFlash 1200, employing the CLIA method. Samples consisted of serum obtained from venous blood, and analyses were performed with internal quality control. The T/C ratio was calculated from the obtained values.

Results

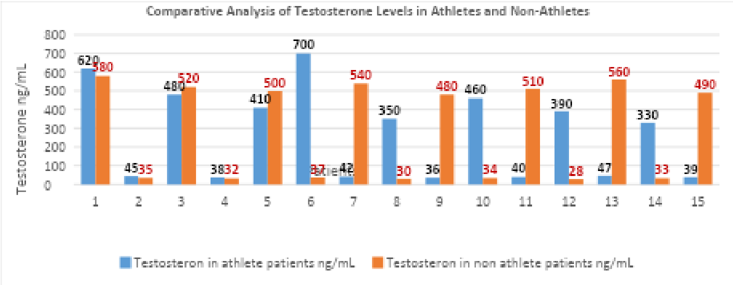
Based on the obtained results regarding metabolic stress, hormonal function, and associated biochemical parameters, the findings are presented in the graphics below:



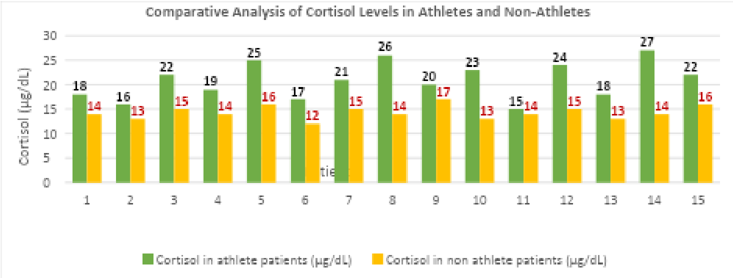
Grafic 1. C-Reactive Protein (CRP) as a Marker of Inflammation in athletes and non athletes (15 first patients are active atheletes and 15 second patients are non athletes)



Grafic 2. Comparison of Creatine Kinase (CK) Levels Between Athletes and Non-Athletes (15 first patients are active atheletes and 15 second patients are non athletes)



Grafic 3. Differences in Testosterone Levels Between Athletes and Non-Athletes



Grafic 4. Differences in Cortisol Levels Between Athletes and Non-Athletes

Table 1: Testosterone/Cortisol (T/C) ratios in athletes and non-athletes

Patient	**Athletes T/C**	**Non-athletes T/C**
1	34.44	41.43
2	2.81	2.69
3	21.82	34.67
4	2	2.29
5	16.4	31.25
6	41.18	3.08
7	2	36
8	13.46	2.14
9	1.8	28.24
10	20	2.62
11	2.67	36.43
12	16.25	1.87
13	2.61	43.08
14	12.22	2.36
15	1.77	30.63

Athletes (T/C ratios)
Values:
34.44, 2.81, 21.82, 2.00, 16.40, 41.18, 2.00, 13.46, 1.80, 20.00, 2.67, 16.25, 2.61, 12.22, 1.77

[1] **Mean = 12.96**
[2] **SD = 12.63**

Athletes: 12.96 ± 12.63
Non-athletes (T/C ratios)
Values:
41.43, 2.69, 34.67, 2.29, 31.25, 3.08, 36.00, 2.14, 28.24, 2.62, 36.43, 1.87, 43.08, 2.36, 30.63

[9] **Mean = 19.79**
[10] **SD = 16.65**
Non-athletes: 19.79 ± 16.65

Discussion

Ethical considerations are of paramount importance when incorporating biomarker analysis in elite sports. Ensuring informed consent, protecting athletes data privacy, and adhering to responsible biomarker data use are essential to uphold athlete rights and wellbeing. Ongoing research and technological innovations may uncover novel biomarkers, providing deeper insights into athlete physiology and performance optimization, further elevating the field of elites ports performance. So the integration of biomarkers in elite sports holds immense promise for optimizing performance and advancing athlete well being. Through objective performance assessments, personalized training strategies, and injury prevention, biomarkers offer invaluable insights that traditional methods cannot provide. Biomarker analysis facilitates evidence based decisions, enabling coaches and sports scientists to fine tune training programs to suit individual athlete responses (Anghel, L.,et al, 2023).

Conclusion

Metabolic stress is a normal consequence of structured athletic training; however, excessive load or inadequate recovery may lead to maladaptive responses and overtraining syndrome. This study highlights key biomarkers, including creatine kinase (CK), cortisol, testosterone, and C-reactive protein (CRP), as objective indicators of athletes physiological and biochemical status under different training conditions. Their combined assessment provides insight into muscle damage, hormonal balance, and systemic inflammation.
The interaction between anabolic and catabolic hormones, together with markers of tissue stress and inflammation, is particularly important for distinguishing adaptive training responses from non-functional overreaching or overtraining. In conclusion, biomarker based monitoring represents a valuable approach for optimizing training load, guiding recovery strategies, and reducing the risk of overtraining, although further research is needed to establish standardized reference values.

References

[1] Seshadri, D.R.; Li, R.T. Wearable Sensors for Monitoring the Internal and External Workload of the Athlete. npjDigit. Med. 2019, 2, 71, doi:10.1038/s41746-019-0149-2 *(PDF) The Role of Biomarkers in Elite Sports*.
[2] Lee, E.C.; Fragala, M.S. Biomarkers in Sports and Exercise: Tracking Health, Performance, and Recovery inAthletes. Journal of Strength and Conditioning Research 2017, 31, 2920–2937, doi:10.1519/JSC.0000000000002122
(PDF) The Role of Biomarkers in Elite Sports.
[3] Pedlar, C.R.; Lewis, N.A. Blood Biomarker Profiling and Monitoring for High-Performance Physiology andNutrition: Current Perspectives, Limitations and Recommendations. Sports Med 2019, 49, 185–198,doi:10.1007/s40279-019-01158-x.
(PDF) The Role of Biomarkers in Elite Sports.
[4] Haller, N.; Behringer, M. Blood-Based Biomarkers for Managing Workload in Athletes: Considerations andRecommendations for Evidence-Based Use of Established Biomarkers. Sports Med 2023, 53, 1315–

1333,doi:10.1007/s40279-023-01836-x.
(PDF) The Role of Biomarkers in Elite Sports.
[5] McFadden, B.A.; Walker, A.J. Biomarkers Correlate With Body Composition and Performance ChangesThroughout the Season in Women's Division I Collegiate Soccer Players. Front. Sports Act. Living 2020, 2, 74,doi:10.3389/fspor.2020.00074
(PDF) The Role of Biomarkers in Elite Sports.
[6] Izquierdo M., Ibañez J., Calbet J.A.L., Navarro-Amezqueta I., González-Izal M., Idoate F., Häkkinen K., Kraemer W.J., Palacios-Sarrasqueta M., Almar M., et al. Cytokine and hormone responses to resistance training. Eur. J. Appl. Physiol. 2009;107:397–409. doi: 10.1007/s00421-009-1139-x. [DOI] [PubMed] [Google Scholar]
[7] Kraemer W.J., Ratamess N.A. Hormonal Responses and Adaptations to Resistance Exercise and Training. Sports Med. 2005;35:339–361. doi: 10.2165/00007256-200535040-00004. [DOI] [PubMed] [Google Scholar]
[8] McDougle J.M., Mangine G.T., Townsend J.R., Jajtner A.R., Feito Y. Acute physiological outcomes of high-intensity functional training: A scoping review. PeerJ. 2023;10:e14493. doi: 10.7717/peerj.14493. [DOI] [PMC free article] [PubMed] [Google Scholar]
[9] Tu H., Li Y.-L. Inflammation balance in skeletal muscle damage and repair. Front. Immunol. 2023;14:1133355. doi: 10.3389/fimmu.2023.1133355. [DOI] [PMC free article] [PubMed] [Google Scholar]
[10] Jiang Q., Lou K., Hou L., Lu Y., Sun L., Tan S.C., Low T.Y., Kord-Varkaneh H., Pang S. The effect of resistance training on serum insulin-like growth factor 1(IGF-1): A systematic review and meta-analysis. Complement. Ther. Med. 2020;50:102360. doi: 10.1016/j.ctim.2020.102360. [DOI] [PubMed] [Google Scholar]
[11] Peake J.M., Neubauer O., Della Gatta P.A., Nosaka K. Muscle damage and inflammation during recovery from exercise. J. Appl. Physiol. 2017;122:559–570. doi: 10.1152/japplphysiol.00971.2016. [DOI] [PubMed] [Google Scholar]
[12] Chycki, J., Krzysztofik, M., Sadowska-Krępa, E., Baron-Kaczmarek, D., Zając, A., Poprzęcki, S., & Petr, M. (2024). Acute Hormonal and Inflammatory Responses following Lower and Upper Body Resistance Exercises Performed to Volitional Failure. *International journal of molecular sciences*, *25*(13), 7455. https://doi.org/10.3390/ijms25137455
[13] Kreher, J.B. & Schwartz, J.B. (2012) Overtraining syndrome: a practical guide. *Sports Health*, 4(2), pp.128–138. https://doi.org/10.1177/1941738111434406
[14] Peake, J.M., Neubauer, O., Della Gatta, P.A. & Nosaka, K. (2017) Muscle damage and inflammation during recovery from exercise. *Journal of Applied Physiology*, 122(3), pp.559–570. https://doi.org/10.1152/japplphysiol.00971.2016
[15] Urhausen, A. & Kindermann, W. (2002) Behavior of testosterone, cortisol and their ratio in response to exercise and training. *Sports Medicine*, 32(15), pp.995–1015. https://doi.org/10.2165/00007256-200232150-00002
[16] Kasapis, C. & Thompson, P.D. (2005) The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *Journal of the American College of Cardiology*, 45(10), pp.1563–1569. https://doi.org/10.1016/j.jacc.2004.12.077
[17] Anghel, L., Gurău, T. V., Gurău, G., Mușat, C. L., Voinescu, D. C., Onu, I., Cordun, M., Codreanu, C.-M., & Iordan, D. A. (2023). *The role of biomarkers in elite sports*.