ORIGINAL SCIENTIFIC PAPER
ORIGINALNI ZNANSTVENI RAD

Hrvat. Športskomed. Vjesn. 2025; 41:21-30

THE DUAL FACE OF SYSTEMIC INFLAMMATION IN CONTACT SPORTS: PATHOLOGICAL RISK OR ADAPTIVE MECHANISM?

DVOSTRUKO LICE SISTEMSKE UPALE U KONTAKTNIM SPORTOVIMA: PATOLOŠKI RIZIK ILI ADAPTIVNI MEHANIZAM?

Alan García Yánez[1], Hernando Baquero Aguilera[1], Kevin Villa Lopera[2], Miguel Mateo Montañez Soler[3]

[1]General Practitioner. Independent Researcher, Sports Medicine Specialization.
Bogotá, Colombia.
[2]Independiente Yumbo FC, Sports Medicine Specialization.
Yumbo, Colombia.
[3]Fortaleza Fútbol Club, Sports Medicine Specialization.
Bogotá, Colombia.

Cite as: Yanez AG, Aguilera HB, Lopera KV, Soler MMM. The dual face of systemic inflammation in contact sports: pathological risk or adaptive mechanism? Croat Sports Med J. 2026; 41(1):21-30.

Corresponding author: Alan García Yánez, imedica.agarciay@gmail.com

DOI: 10.69589/hsv.41.1.3

ABSTRACT

Systemic inflammation represents a defining yet paradoxical hallmark of athletes participating in contact sports. Repetitive mechanical trauma, impact-induced muscle damage, and concussive or sub-concussive head impacts elicit inflammatory responses that may function either as adaptive signaling mechanisms or as drivers of long-term pathology. On one hand, transient and well-regulated inflammatory cascades support skeletal muscle repair, metabolic remodeling, angiogenesis, and neuroplasticity, thereby facilitating training adaptation and performance enhancement. On the other hand, unresolved or excessive inflammation promotes cumulative tissue damage, accelerates musculoskeletal degeneration, disrupts immune and neuroendocrine homeostasis, and contributes to neurocognitive decline, ultimately increasing injury risk and shortening athletic career longevity.

This narrative review synthesizes current experimental, clinical, and translational evidence examining the bidirectional role of systemic inflammation in contact sport athletes. Particular emphasis is placed on the molecular and cellular mechanisms linking mechanical trauma to immune activation, including damage-associated molecular patterns, pattern-recognition receptor signaling, cytokine cascades, and impaired inflammatory resolution. Furthermore, the review explores how chronic low-grade inflammation intersects with overtraining syndrome,

SAŽETAK

Sistemska upala predstavlja obilježje sportaša koji sudjeluju u kontaktnim sportovima koje je istodobno definirajuće i paradoksalno. Ponavljana mehanička trauma, oštećenje mišića uzrokovano udarcima te kontuzijski I subkontuzijski udarci u glavu izazivaju upalne odgovore koji mogu djelovati ili kao adaptivni signalni mehanizmi ili kao pokretači dugoročne patologije. S jedne strane, prolazni i dobro regulirani upalni procesi podupiru popravak skeletnih mišića, metaboličko remodeliranje, angiogenezu i neuroplastičnost, čime omogućuju adaptaciju na trening i poboljšanje sportske izvedbe. S druge strane, nerazriješena ili pretjerana upala potiče kumulativno oštećenje tkiva, ubrzava muskuloskeletnu degeneraciju, narušava imunološku i neuroendokrinu homeostazu te doprinosi neurokognitivnom propadanju, povećavajući rizik od ozljeda i skraćujući trajanje sportske karijere.

Ovaj narativni pregled sintetizira postojeće eksperimentalne, kliničke i translacijske dokaze o dvosmjernoj ulozi sistemske upale u sportaša kontaktnih sportova. Poseban naglasak stavljen je na molekularne i stanične mehanizme koji povezuju mehaničku traumu s imunološkom aktivacijom, uključujući signalizaciju putem molekula povezanih s oštećenjem, receptora urođene imunosti, citokinske kaskade i poremećenu rezoluciju upale. Također se razmatra povezanost kronične niskogradijentne upale s sindromom pretreniranosti, imunosupresijom, immune suppression, cardiovascular dysfunction, and neurodegenerative processes associated with repetitive head impacts.

Key circulating biomarkers—including interleukin-6, tumor necrosis factor-α, C-reactive protein, creatine kinase, and neurofilament light chain—are discussed as practical tools for distinguishing adaptive inflammatory responses from maladaptive trajectories. Their interpretation is framed within the context of training load, recovery intervals, individual biological variability, and cumulative exposure to contact-related trauma. Finally, the review highlights emerging precision-based strategies aimed at modulating systemic inflammation, integrating longitudinal biomarker monitoring, genetic and microbiome profiling, and targeted recovery interventions.

Understanding the dual nature of systemic inflammation is essential for optimizing athletic performance while safeguarding long-term health. When appropriately regulated, inflammation constitutes a cornerstone of physiological adaptation; when dysregulated, it becomes a central mediator of injury, disease risk, and premature performance decline. Future approaches in sports medicine should therefore focus on individualized strategies to tilt the inflammatory balance toward adaptation, resilience, and athlete longevity.

Keywords: *Inflammation, Athletes, Sports Injuries, Contact Sports.*

kardiovaskularnom disfunkcijom i neurodegenerativnim procesima povezanim s ponavljanim udarcima u glavu.

Ključni cirkulirajući biomarkeri, uključujući interleukin-6, faktor nekroze tumora-α, C-reaktivni protein, kreatin-kinazu i laki lanac neurofilamenta prikazani su kao praktični alati za razlikovanje adaptivnih i patoloških upalnih odgovora. Njihova interpretacija razmatra se u kontekstu opterećenja treningom, intervala oporavka, individualne biološke varijabilnosti i kumulativne izloženosti kontaktnoj traumi. U zaključku se naglašavaju precizne strategije koje integriraju longitudinalno praćenje biomarkera, genetsko i mikrobiomsko profiliranje te ciljane intervencije oporavka s ciljem usmjeravanja upalne ravnoteže prema adaptaciji, otpornosti i dugovječnosti sportaša.

Ključne riječi: *Upala, sportaši, sportske ozljede, kontaktni sportovi*

1. INTRODUCTION

Systemic inflammation in athletes engaged in contact sports arises from repetitive head impacts, exercise-induced muscle damage, and alterations in peripheral systems [1]. Concussive and sub-concussive blows trigger neuroinflammatory cascades involving blood–brain barrier dysfunction, cerebral edema, and biomarker release (e.g., S-100B). Both animal and clinical studies show robust responses characterized by astrogliosis, microgliosis, and cytokine shifts, with elevations in TNF-α and IL-6 and reductions in IL-10 [1,56,60].

Beyond the central nervous system, high-intensity exercise amplifies systemic inflammation. Microtrauma in skeletal muscle promotes cytokine release (IL-1β, IL-6), further modulated by metabolic hormones such as leptin, ghrelin, and adiponectin [24,28,45]. Emerging evidence highlights gut–brain–immune interactions, with concussed athletes showing microbiome alterations, including loss of anti-inflammatory species like Eubacterium rectale and Anaerostipes hadrus, suggesting dysbiosis sustains inflammation [11,15].

Chronic exposure to head trauma may establish persistent low-grade inflammation linked to long-term sequelae, including chronic traumatic encephalopathy, autonomic dysfunction, and increased risk of cardiovascular disease [14,35]. Biomarkers such as S-100B and neurofilament light chain provide insight into axonal injury, but systemic characterization remains limited, as most studies focus on neurological outcomes [1,46]. Inflammatory responses depend on trauma and exercise parameters, recovery intervals, and cumulative exposures, which may yield either adaptive or detrimental effects [37, 64]. Novel approaches, including saliva microRNAs and multiplex biomarker panels, offer promise for minimally invasive monitoring [32, 23,51,43].

In sports medicine, systemic inflammation is recognized as a dual-edged process [19,28,33]. Adaptive inflammation supports tissue repair and performance, with muscle micro-damage triggering macrophage infiltration that shifts from M1 to M2 phenotype, enabling healing and remodeling [9,15,19]. Neuroendocrine regulation via the sympathetic nervous system and HPA axis balances cytokine activity, while muscle-derived IL-6 exerts anti-inflammatory effects by promoting IL-10 and IL-1 receptor antagonist, independent of TNF-α [3,10,29, 31].

By contrast, pathological inflammation emerges when this balance fails, leading to chronic cytokine elevation, impaired regeneration, insulin resistance, and systemic disease risk (2,3,7,16). This maladaptive state involves prolonged immune activation, oxidative stress, and disrupted tolerance, heightening susceptibility to poor recovery and chronic disease (5,34,50).

Thus, systemic inflammation in contact sports represents both an adaptive mechanism fostering recovery and a pathological process predisposing athletes to long-term health risks.

2. MECHANISMS OF SYSTEMIC INFLAMMATION IN CONTACT SPORTS

Repeated musculoskeletal trauma in contact sports triggers systemic inflammation through interconnected molecular and cellular mechanisms driven by mechanical and biochemical tissue damage. Mechanical overload, blunt-force impacts, and repetitive joint trauma disrupt muscle membranes and joint structures, leading to the release of intracellular components and extracellular matrix fragments. These damage-associated molecular patterns (DAMPs), including collagen fragments and matrix degradation products, act as endogenous danger signals that initiate inflammatory responses (7,10,15, 36).

DAMPs are detected by pattern recognition receptors (PRRs), such as Toll-like receptors (TLR2 and TLR4), the receptor for advanced glycation end products (RAGE), and nucleotide-binding oligomerization domain-like receptors (NLRs) expressed on immune and connective tissue cells. Activation of these receptors triggers intracellular signaling cascades converging on transcription factors including nuclear factor-κB (NF-κB), activator protein-1 (AP-1), and cAMP response element-binding protein (CREB). This signaling promotes the production of proinflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α) and chemokines, amplifying local and systemic immune activation (27,48). Persistent NF-κB activation following repetitive trauma sustains the inflammatory milieu characteristic of contact sport athletes (5,7,9,18,56).

The early inflammatory phase is marked by rapid recruitment of neutrophils and monocytes. Neutrophils release proteases and reactive oxygen species (ROS), exacerbating tissue injury, while macrophages reinforce inflammation through cytokine and growth factor secretion (8,10,11,12,15,26). In joint tissues, matrix metalloproteinases (MMP-3 and MMP-13) and ADAMTS proteases accelerate cartilage degradation, and extracellular matrix proteins such as tenascin-C—upregulated by mechanical overload—further propagate inflammatory signaling via TLR4 activation (14,26).

Oxidative stress represents an additional driver of tissue pathology. Excessive ROS accumulation damages lipids, proteins, and DNA, while activation of the NLRP3 inflammasome promotes caspase-1–dependent maturation of IL-1β and IL-18. When counter-regulatory mechanisms, including IL-10 and the IL-1 receptor antagonist, are overwhelmed, inflammation shifts toward a persistent proinflammatory state associated with chronic inflammation and post-traumatic osteoarthritis (29).

Recurrent injury perpetuates cycles of immune activation and oxidative stress that may extend beyond musculoskeletal tissues, contributing to neuroinflammatory processes following concussive and sub-concussive impacts, including microglial activation and blood–brain barrier disruption (13,17,19).

Inflammatory responses in contact sports differ fundamentally from those in endurance or non-contact activities. Impact-induced muscle damage (IIMD) in contact sports results from direct mechanical trauma and elicits an immediate and robust inflammatory response, characterized by early mast cell and neutrophil activation, rapid release of proinflammatory mediators, and delayed macrophage polarization toward anti-inflammatory phenotypes (8,10,13,16). In contrast, endurance exercise primarily induces exercise-induced muscle damage (EIMD) driven by eccentric contractions and metabolic stress, leading to a more regulated inflammatory response dominated by transient IL-6 elevations that facilitate muscle repair and adaptation (28,45,63).

The cumulative inflammatory burden in contact sports extends beyond muscle tissue. Impact-related vascular injury and transient ischemia promote edema, hematoma formation, and prolonged neutrophil infiltration, often delaying recovery compared with endurance sports (5,9,19,27). Accordingly, athletes in contact sports frequently exhibit persistently elevated systemic inflammatory markers, including IL-8, CCL-2, IL-2, and vascular cell adhesion molecule-1 (VCAM-1), suggesting a chronic low-grade inflammatory state that exceeds acute recovery windows. In contrast, inflammatory responses in non-contact sports are typically transient and more closely linked to exercise load than to mechanical trauma (3,9,61,64).

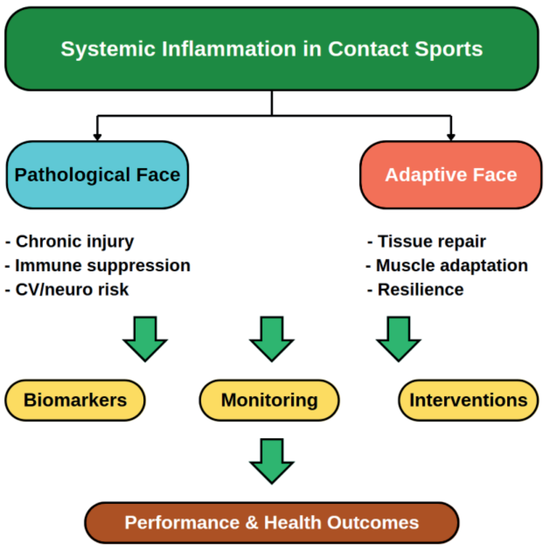

Figure 1. Conceptual framework of systemic inflammation in contact sports.

Slika 1. Konceptualni okvir sistemske upale u kontaktnim sportovima

Together, these mechanisms illustrate how contact sports uniquely drive systemic inflammation through recurrent cycles of mechanical injury, immune activation, and impaired inflammatory resolution, distinguishing them from the predominantly adaptive inflammatory responses observed in non-contact athletic activities.

3. PATHOLOGICAL FACE: SYSTEMIC INFLAMMATION AS A RISK FACTOR

3.1. Evidence linking chronic systemic inflammation to overuse injuries and long-term musculoskeletal damage

Chronic systemic inflammation has emerged as a central mediator in the pathogenesis of overuse injuries and long-term musculoskeletal deterioration among athletes participating in contact sports. In contrast to the acute and transient inflammatory responses required for effective tissue healing, persistent low-grade inflammation establishes a pathological environment that disrupts regenerative processes, compromises tissue integrity, and promotes cumulative injury over time.

One of the key mechanisms underpinning this process involves the gut–musculoskeletal axis. Repeated physical stress, dietary imbalances, and environmental exposures may induce gut dysbiosis and increased intestinal permeability, commonly referred to as "leaky gut syndrome." Disruption of the intestinal barrier facilitates the translocation of bacterial toxins and endotoxins into the systemic circulation, precipitating a chronic inflammatory state characterized by sustained elevations of pro-inflammatory cytokines [(14,21,28,30)]. This systemic inflammatory burden impairs muscle recovery, regeneration, and protein synthesis, thereby predisposing athletes to acute muscle soreness, recurrent injuries, and, in severe cases, progressive muscle wasting. Importantly, interventions targeting gut microbiota—such as probiotic supplementation and dietary modulation—have shown potential to restore intestinal barrier function, attenuate systemic inflammation, and indirectly enhance musculoskeletal resilience [(7,11,60,62)].

At the local tissue level, overuse injuries including tendinopathies and post-traumatic osteoarthritis exemplify the concept of a "failed healing response." In these conditions, cytokines such as TNF-α, IL-6, IL-1β, and monocyte chemoattractant protein-1 (MCP-1) accumulate persistently within the injured microenvironment [(21,29,50)]. Sustained cytokine activity disrupts the balance between anabolic and catabolic signaling by promoting fibroblast proliferation, aberrant collagen deposition, and extracellular matrix disorganization. Rather than supporting adaptive remodeling, these processes culminate in fibrosis, reduced regenerative capacity, and chronic pain, effectively shifting tissue repair toward pathological remodeling.

Systemic inflammation also undermines skeletal muscle anabolic responses. In contact sport athletes, an elevated baseline inflammatory status—often assessed using indices such as the neutrophil-to-lymphocyte ratio—has been associated with blunted training adaptations, including attenuated improvements in aerobic performance and unfavorable changes in body composition [(2,11,19,28,51)]. From a mechanistic perspective, this reflects a disrupted anabolic–catabolic hormonal balance that constrains effective muscle regeneration and recovery.

Oxidative stress further amplifies this pathological cascade. Excessive production of reactive oxygen species (ROS), particularly during repetitive ischemia–reperfusion cycles inherent to high-intensity contact activities, accelerates oxidative modification of collagen and extracellular matrix proteins [(9,14,17,57)]. These structural alterations weaken tendons and cartilage, reduce their tolerance to mechanical loading, and predispose tissues to progressive degenerative change.

Although large-scale genomic analyses have reported limited direct associations between chronic inflammation and overuse injuries [(21,29,38)], converging evidence from mechanistic, translational, and clinical studies strongly supports chronic systemic inflammation as a key driver of connective tissue degeneration, impaired repair, and musculoskeletal vulnerability in contact sport athletes [(7,27,31,54)]. Collectively, findings related to the gut–musculoskeletal axis, cytokine dysregulation, oxidative stress, and hormonal imbalance underscore systemic inflammation as a major pathological determinant of long-term musculoskeletal damage.

3.2. Immune Dysregulation and Overtraining

Systemic inflammation in contact sports is largely initiated by repeated high-intensity exercise and tissue trauma, which stimulate the release of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β) from activated immune cells [(3,30,41,53)]. While these mediators are essential for acute tissue repair, their sustained elevation promotes widespread immune activation that may evolve into a chronic inflammatory state. Prolonged cytokine exposure disrupts hypothalamic–pituitary–adrenal (HPA) axis regulation and alters glucocorticoid secretion patterns, creating a physiological milieu characterized by immune suppression and impaired homeostasis [(41,56,61)].

Periods of intense training further exacerbate this maladaptation through increased secretion of stress hormones, including cortisol and catecholamines. Elevated cortisol levels directly suppress key immune functions, such as macrophage phagocytic activity, neutrophil degranulation, lymphocyte proliferation, and antibody production [(30,32,38,45)]. Clinical studies in elite athletes exposed to congested competition schedules consistently report neutrophilia, lymphocytopenia, and elevated neutrophil-to-lymphocyte ratio (NLR), all of which are indicative of transient immunosuppression [(29,33,34)].

This immune imbalance generates an "open window" of vulnerability to infections, particularly affecting the upper respiratory tract. Reductions in mucosal immune defenses, most notably salivary immunoglobulin A (IgA), further compromise first-line protection against airborne pathogens, thereby increasing infection risk during and following periods of high training or competitive load [8,16,22,25].

Over time, persistent systemic inflammation contributes to the development of overtraining syndrome (OTS), a multifactorial condition characterized by chronic fatigue, performance decline, and psychological disturbances. Sustained cytokine signaling interferes with neuroendocrine and immune–brain–muscle communication, impairing energy metabolism, tissue repair, and recovery capacity [54,62]. This maladaptive state is reinforced by altered leukocyte profiles, including lymphocytopenia and imbalances in T-cell subsets, reflecting compromised adaptive immune function [26,29,31,33,63].

Alterations in gut microbiota further compound immune dysregulation. Intense physical activity and contact-related stressors reduce microbial diversity and beneficial bacterial populations, promoting dysbiosis and increased intestinal permeability. These changes exacerbate systemic inflammation, impair natural killer cell activity, suppress both T- and B-cell responses, and further reduce salivary IgA secretion [5,19,27,48]. The gut–immune axis therefore acts as both a driver and amplifier of systemic inflammation, contributing to immune vulnerability and the pathophysiology of OTS [34,39,47].

Additional modulating factors, including psychological stress, inadequate sleep, and nutritional deficiencies, amplify neuroendocrine stress responses and sustain inflammatory activity [5,9,17,27]. Targeted interventions—such as nutritional optimization, probiotic supplementation, and the use of anti-inflammatory micronutrients—have shown promise in mitigating these maladaptations, restoring immune balance, and reducing infection risk in highly trained athletes [31,38,47,52].

3.3. Neurocardiovascular Sequelae of Systemic Inflammation

Beyond immune and metabolic dysregulation, systemic inflammation has been increasingly implicated in cardiovascular and neurodegenerative sequelae associated with repetitive head trauma. Mechanical insults activate microglia and astrocytes, leading to the release of pro-inflammatory cytokines (e.g., IL-1, IL-2, IL-8) and chemokines (e.g., CCL-2, CCL-3), which establish a chronic neuroinflammatory environment that may persist long after the acute injury phase [7,11,19,61]. Elevated systemic inflammatory markers, such as C-reactive protein (CRP) and intercellular adhesion molecule-1 (ICAM-1), have been associated with endothelial dysfunction, persistent vascular injury, and adverse vascular remodeling, ultimately increasing cardiovascular disease risk [5,15,58].

Sustained neuroinflammation also accelerates neurodegenerative cascades. Traumatic axonal injury promotes calcium influx, excitotoxicity, and kinase activation, leading to tau hyperphosphorylation and deposition of amyloid-β aggregates—pathological hallmarks of chronic traumatic encephalopathy (CTE) and Alzheimer's disease (AD) [3,9,25,30,34]. Persistent microglial activation further impairs protein clearance and facilitates the propagation of tau pathology, establishing a mechanistic link between repetitive trauma and long-term neurocognitive decline [4,39,41].

Neuropathological evidence indicates that cumulative exposure to head impacts correlates with increased microglial activation and tau aggregation, suggesting a dose–response relationship between inflammatory burden and neurodegeneration [11,16,53,60]. Moreover, cerebrospinal fluid biomarkers, including elevated IL-6 concentrations, have been associated with behavioral dysregulation and cognitive impairment in retired contact sport athletes, reinforcing the systemic–neuroinflammatory connection [51,58].

Collectively, these findings identify systemic inflammation as a central pathological nexus linking repetitive physical trauma to immune suppression, increased infection susceptibility, overtraining syndrome, cardiovascular dysfunction, and neurodegenerative outcomes in athletes engaged in contact sports.

4. ADAPTIVE FACE: INFLAMMATION AS A MECHANISM OF REMODELING

Acute systemic inflammation constitutes a fundamental biological mechanism that coordinates tissue repair and structural adaptation following the repetitive trauma inherent to contact sports [28,36,41,49]. This response is initiated by the release of pro-inflammatory cytokines such as TNF-α, IL-1, and IL-6 from damaged tissues, which rapidly recruit neutrophils and monocytes to the injury site [6,61,57,59]. These immune cells clear necrotic debris and potential pathogens, establishing a regenerative microenvironment that supports subsequent repair processes [7,18,59,63].

Beyond debris clearance, acute inflammation actively stimulates regenerative pathways. In skeletal muscle, low-level TNF-α signaling promotes satellite cell activation and myofiber regeneration, while in bone, inflammatory mediators enhance mesenchymal stem cell migration and callus mineralization [15,28,39,46]. In this context, inflammation functions as a biological bridge that translates mechanical injury into regenerative activation.

The transition from inflammation to resolution is tightly regulated by lipid mediators. Pro-inflammatory eicosanoids, including prostaglandins and leukotrienes, interact with specialized pro-resolving mediators such as resolvins, protectins, and lipoxins to control protein turnover and extracellular matrix remodeling [3,16,47]. This coordinated sequence fosters a pro-anabolic environment, supporting angiogenesis, fibroblast activity, collagen deposition, and vascular remodeling through growth factors such as VEGF and TGF-β [31,39,47,51].

The adaptive nature of inflammation is further illustrated by the repeated bout effect. Following initial contact-induced muscle damage, subsequent exposures elicit attenuated inflammatory responses accompanied by improved neuromuscular performance and reduced biochemical markers of tissue damage [16,52,56]. This phenomenon highlights how transient inflammation conditions tissues for resilience against recurrent mechanical stress.

Importantly, effective adaptation depends on precise inflammatory regulation. Excessive suppression of acute inflammation, such as through high-dose non-steroidal anti-inflammatory drugs or excessive antioxidant intake, has been shown to impair satellite cell activity, blunt anabolic signaling, and delay tissue regeneration [16,37,49,51]. Conversely, inadequate inflammatory signaling compromises immune cell recruitment and weakens myogenic responses, underscoring the necessity of an intact but controlled inflammatory cascade for efficient repair [38,60].

Thus, the duality of inflammation lies not in its presence, but in its regulation. A robust yet transient inflammatory response provides essential signals for muscle hypertrophy, angiogenesis, and extracellular matrix remodeling, while timely resolution—mediated by macrophage polarization from M1 to M2 phenotypes and increased IL-10 and TGF-β secretion—prevents fibrosis and promotes tissue integration [51,53,63]. Chronic training further shifts this balance toward a protective anti-inflammatory profile, characterized by reduced pro-inflammatory cytokines and elevated adiponectin levels in well-trained athletes [2,24,28,64].

Ultimately, acute inflammation in contact sports should be viewed as an indispensable adaptive mechanism rather than solely a pathological risk. When appropriately regulated, inflammatory signaling enables tissue recovery to evolve into structural and functional enhancement, forming the biological foundation of resilience and long-term adaptation to high-impact athletic demands [2,14,42,53].

5. BIOMARKERS OF SYSTEMIC INFLAMMATION IN CONTACT SPORTS

Biomarker assessment has become central to understanding systemic inflammation in contact sport athletes, providing insight into both adaptive and pathological inflammatory states. Among available markers, interleukin-6 (IL-6) and C-reactive protein (CRP) are the most reliable and widely validated. IL-6 rises rapidly following acute muscle damage, concussion, or intense exertion, making it a sensitive marker of early inflammatory activation [4,15,54]. In contrast, CRP—synthesized by the liver in response to IL-6—exhibits delayed but sustained elevation, reflecting cumulative inflammatory burden and recovery trajectory [14,34,55]. High-sensitivity CRP (hsCRP) further allows detection of subtle inflammatory fluctuations during heavy training or post-injury periods [26,29,34,55].

Other cytokines provide complementary information but with greater variability. TNF-α may be elevated in acute inflammatory states and mild traumatic brain injury, yet its interpretation is influenced by exercise intensity, training adaptation, and sampling timing, limiting its utility as a standalone marker [15,29,34,56]. Conversely, interleukin-10 (IL-10) reflects the resolution phase of inflammation and offers prognostic insight into the balance between pro- and anti-inflammatory signaling when interpreted alongside IL-6 and CRP [26,29,57,58].

Beyond cytokines, biomarker interpretation is influenced by individual factors such as age, sex, training load, and genetic background. Hormonal markers (e.g., cortisol, testosterone) and muscle damage indicators (creatine kinase, CK) show substantial interindividual variability, necessitating longitudinal monitoring and individualized baselines [35,38,59,60]. Sex-specific differences further modulate responses, with estrogen attenuating CK elevations in female athletes and testosterone-to-cortisol ratios reflecting anabolic–catabolic balance [34,37,60,63]. Developmental stage also influences recovery kinetics in younger athletes [29,52,56].

Effective monitoring therefore relies on integrated, multi-marker strategies. Adaptive inflammation is characterized by transient IL-6 elevations and short-lived CK peaks, whereas sustained CRP elevation, persistently high CK, or altered immune indices such as an elevated neutrophil-to-lymphocyte ratio (NLR) indicate maladaptive inflammation, overtraining, or immune suppression [24,44,55]. Additional markers, including myeloperoxidase, lactate dehydrogenase, and salivary immunoglobulin A, further refine risk stratification, with low salivary IgA consistently associated with increased infection susceptibility [14,39,63].

The most robust monitoring frameworks integrate longitudinal, multi-marker profiles using standardized laboratory and point-of-care techniques to detect deviations from individual baselines. Such multidimensional approaches enhance the ability to distinguish beneficial inflammatory adaptation from pathological overload, supporting informed decision-making in training, recovery, and athlete health management [28,37,49,64].

6. MONITORING AND INTERVENTIONS

Effective modulation of systemic inflammation in contact sports requires an integrated and individualized approach, given athletes' repeated exposure to high mechanical loads, muscle damage, and inflammatory stress. Optimal strategies combine training load management, targeted nutrition, recovery modalities, and judicious use of pharmacological and non-pharmacological interventions to support tissue repair and limit maladaptation.

Training load management is the primary determinant of inflammatory control. Excessive microtrauma and

Table 1. Comparative Summary: Adaptive vs. Pathological Biomarker Profiles in Contact Sports.
Tablica 1. Komparativni sažetak: adaptivni nasuprot patološkim biomarkernim profilima u kontaktnim sportovima

Dimension	Adaptive Inflammation	Pathological Inflammation
Cytokines	Transient IL-6 elevation post-exercise, signaling muscle repair and metabolic adaptation.	Sustained elevation of IL-6 and TNF-α, reflecting unresolved inflammation and immune dysregulation.
Acute-Phase Proteins	Mild or short-lived CRP increase, aligning with transient tissue repair.	Persistent CRP or hsCRP elevation, indicating chronic inflammatory load and systemic stress.
Anti-Inflammatory Cytokines	IL-10 increase during recovery, facilitating resolution of inflammation.	Blunted or insufficient IL-10 response, impairing recovery and balance of immune signaling.
Hormonal Markers	Transient cortisol rise with rapid normalization; balanced testosterone/cortisol ratio supports recovery.	Chronic cortisol elevation, reduced testosterone/cortisol ratio, sustained catabolic dominance.
Muscle Damage Markers	CK and LDH show rapid but reversible peaks (24–48h) consistent with adaptive remodeling.	Persistently elevated CK and LDH, signaling unresolved muscle damage and overtraining.
Immune Function Indicators	Stable or mildly reduced salivary IgA (s-IgA), quick recovery of mucosal immunity.	Sustained s-IgA suppression, increased infection susceptibility, higher incidence of URTIs.
Immune Cell Indices	Normal or transient shifts in neutrophil-to-lymphocyte ratio (NLR) post-exercise.	Persistently elevated NLR and lymphocytopenia, indicating immune suppression.
Gut–Immune Axis	Preserved microbial diversity, balanced gut permeability, and normal NK/T-cell activity.	Dysbiosis with reduced microbial diversity, increased permeability, impaired NK/T-cell responses.
Outcome	Enhanced adaptation, tissue repair, and performance gains with adequate recovery.	Overtraining syndrome, heightened infection risk, cardiometabolic dysfunction, neurodegeneration.

unmonitored overreaching promote chronic inflammation and contribute to overtraining syndrome. Gradual progression of training volume and intensity, combined with structured recovery periods and active recovery sessions, facilitates tissue remodeling while minimizing prolonged cytokine elevation [11,17,47, 58].

Nutrition plays a central regulatory role. Carbohydrate intake during prolonged exercise attenuates hypothalamic–pituitary–adrenal axis activation and reduces IL-6 release, while adequate protein intake supports muscle repair and limits exercise-induced muscle damage [39,56,59]. Diets enriched with omega-3 fatty acids, polyphenols, and vitamin D further reduce oxidative stress and promote inflammatory resolution.

Recovery modalities such as cold-water immersion and cryotherapy reduce secondary tissue damage and delayed-onset muscle soreness by limiting neutrophil infiltration and local inflammation [14,28,29,45,58]. Alternating heat and cold exposure may additionally support pro-resolving inflammatory pathways. Protective equipment and mechanical strategies reduce impact-related trauma, lowering overall inflammatory burden [16,28,33,49].

Pharmacological agents, particularly NSAIDs, effectively reduce pain and acute inflammation but may impair anabolic signaling and tissue remodeling when used excessively or chronically [14,22,36,60]. Their use should therefore be limited, context-specific, and carefully monitored due to potential gastrointestinal, renal, and cardiovascular risks [45,48,51].

Non-pharmacological strategies aim to preserve the adaptive role of inflammation. Combined aerobic and resistance training promotes transient inflammatory responses necessary for adaptation while supporting long-term anti-inflammatory profiles. Stress-management techniques, anti-inflammatory dietary patterns, and probiotic supplementation further contribute to immune balance and reduced infection risk [24,27,48,63].

Overall, inflammation management in contact sports must be context-specific and individualized to ensure that inflammatory signaling supports adaptation rather than pathological overload.

7. CLINICAL AND PERFORMANCE IMPLICATIONS

Systemic inflammation in contact sports has major implications for performance, injury risk, and career longevity. Poorly regulated inflammatory responses—

Table 2. Clinical-Comparative Summary: Adaptive vs. Pathological Inflammation in Contact Sports.
Tablica 2. Kliničko-komparativni sažetak: adaptivna nasuprot patološkoj upali u kontaktnim sportovima

Domain	Adaptive Inflammation	Pathological Inflammation	Key Biomarkers
Performance	Enhances recovery and adaptation; promotes mitochondrial biogenesis, improved glucose/lipid metabolism; transient fatigue followed by supercompensation.	Chronic fatigue, reduced aerobic capacity, impaired muscle contractility; risk of overtraining syndrome (OTS).	IL-6 (transient ↑), lactate clearance, ROS–antioxidant balance vs. chronically ↑ TNF-α, cortisol, persistent high CRP.
Musculoskeletal Injuries	Supports tissue remodeling and repair (collagen synthesis, angiogenesis); controlled inflammation accelerates healing.	Delayed recovery, chronic tendinopathies, joint degeneration, fibrosis, higher risk of re-injury.	Transient ↑ CK, MMPs (regulated) vs. persistent ↑ CRP, IL-1β, SAA, uncontrolled MMP activity.
Neurocognition	Transient neuroinflammation facilitating synaptic plasticity and repair; neurotrophic support (BDNF ↑).	Chronic neuroinflammation, microglial hyperactivation, tauopathy, cognitive decline, ↑ risk of CTE.	Controlled ↑ IL-6, BDNF vs. chronic ↑ TNF-α, IL-1β, p-Tau, neurofilament light chain (NfL).
Longevity in Sport	Balanced inflammation promotes adaptation, injury resilience, and prolonged high-level performance.	Accelerated aging of tissues, vascular dysfunction, neurodegeneration, premature sport retirement.	Adaptive cytokine cycling, normal endothelial function vs. persistent ↑ VCAM-1, ICAM-1, arterial stiffness indices, dysbiosis markers (LPS).

driven by repetitive trauma, congested competition schedules, and insufficient recovery—impair muscle regeneration, prolong fatigue, and limit peak performance capacity [26,39,60].

While acute inflammation is essential for tissue repair, unresolved inflammatory activity sustains elevations in IL-6, TNF-α, creatine kinase, and C-reactive protein, delaying recovery and increasing susceptibility to overuse injuries and recurrent soft-tissue damage [55,58,60]. Chronic inflammation also contributes to immune suppression, heightening infection risk and compounding musculoskeletal deterioration [11,19,26,64].

Neurological health is particularly affected. Repetitive concussive and sub-concussive impacts trigger neuroinflammatory processes associated with microglial activation, astrocytic reactivity, and elevations in tau protein and neurofilament light chain. Neuroimaging studies reveal structural brain alterations even in asymptomatic athletes, linking chronic inflammation to cognitive decline and increased risk of chronic traumatic encephalopathy [15,56,60].

Genetic susceptibility and gut-derived inflammation further modulate individual inflammatory responses, influencing recovery capacity and tissue vulnerability [14,43,61]. Over time, cumulative inflammatory burden leads to reduced performance consistency, increased injury incidence, accelerated degenerative changes, and shortened athletic careers, with long-term consequences extending beyond sport to cardiovascular and metabolic health [24,49,63].

Targeted, individualized strategies—particularly omega-3 supplementation, biomarker-guided monitoring, and personalized training and recovery plans—are essential to mitigate these risks, preserve performance, and extend athletic longevity [7,17,29,33,37].

8. CONCLUSIONS

Systemic inflammation in contact sports embodies a dual nature: it is both an indispensable driver of physiological adaptation and a potent mediator of pathological decline. When balanced, inflammatory signaling orchestrates tissue repair, metabolic remodeling, and resilience, ultimately enhancing performance and prolonging career longevity. However, when unresolved or excessive, the same pathways accelerate musculoskeletal degeneration, impair neurocognitive function, and compromise long-term health. Recognizing this duality is central to clinical practice and sports medicine research. The future lies in precision strategies (integrating biomarker profiling, genetic screening, and individualized recovery protocols) to shift the inflammatory balance toward adaptation while mitigating the risks of chronic pathology.

References

1. Aicale R, Tarantino D, Maffulli N. Overuse injuries in sport: a comprehensive overview. J Orthop Surg Res. 2018;13(1):309.
2. Álvarez-Herms J, González A, Corbi F, Odriozola I, Odriozola A. Possible relationship between the gut leaky syndrome and musculoskeletal injuries: the important role of gut microbiota as indirect modulator. AIMS Public Health. 2023;10(3):710.
3. Anghel L, Gurau TV, Gurau G, Mușat CL, Voinescu DC, Onu I, et al. The role of biomarkers in elite sports. Balneo PRM Res J. 2023;14(3):581.
4. Armstrong LE, Bergeron MF, Lee EC, Mershon JE, Armstrong EM. Overtraining syndrome as a complex systems phenomenon. Front Netw Physiol. 2022;1:794392.
5. Baker C, Hunt J, Piasecki J, Hough J. Lymphocyte and dendritic cell response to intensified training in humans and rodents: a systematic review and meta-analysis. Front Physiol. 2022;13:998925.
6. Barbe MF, Lambi AG, Harris MY, Patel PR, Tamas IP, McGonagle ER, et al. Overuse injury induces persistent behavioral declines associated with increased IL-6 expression. Front Physiol. 2025;16:1500795.
7. Bennett JM, Reeves G, Billman GE, Sturmberg JP. Inflammation—nature's way to respond to challenges: implications for chronic disease management. Front Med. 2018;5:316.
8. Bolger C, Mara J, Pyne DB, McKune AJ. Beyond the hit: muscle and vascular tissue responses to contact exposure in collision sports—a narrative review. Sports Med. 2025;1–19.
9. Bozzini BN. Athlete-monitoring to assess performance, biomarker responses, and training load in female collegiate athletes [doctoral dissertation]. Rutgers University; 2020.
10. Buonocore D, Negro M, Arcelli E, Marzatico F. Anti-inflammatory dietary interventions and supplements to improve performance during athletic training. J Am Coll Nutr. 2015;34(Suppl 1):62–7.
11. Celeski M, Segreti A, Crisci F, Cricco R, Piscione M, Di Gioia G, et al. Cardiac troponin and emerging biomarkers among athletes. Biomolecules. 2024;14(12):1630.
12. Chazaud B. Inflammation during skeletal muscle regeneration and tissue remodeling. Immunol Cell Biol. 2016;94(2):140–5.
13. Chen CY, Liao YH, Chou CC, Sung YC, Tsai SC. Initial systemic inflammatory state perturbs training adaptations in elite taekwondo athletes. PLoS One. 2017;12(4):e0176140.
14. Cherry JD, Tripodis Y, Alvarez VE, Huber B, Kiernan PT, Daneshvar DH, et al. Microglial neuroinflammation contributes to tau accumulation in chronic traumatic encephalopathy. Acta Neuropathol Commun. 2016;4(1):112.
15. Crescioli C. Vitamin D, exercise, and immune health in athletes. Front Immunol. 2022;13:954994.
16. DeKosky ST, Asken BM. Injury cascades in TBI-related neurodegeneration. Brain Inj. 2017;31(9):1177–82.
17. Dinetz E, Bocharova N. Inflammation in elite athletes: novel factors, microbiome, and treatments for performance longevity. Cureus. 2024;16(10).
18. Duchesne E, Dufresne SS, Dumont NA. Impact of inflammation and anti-inflammatory modalities on skeletal muscle healing. Phys Ther. 2017;97(8):807–17.
19. Fatouros IG, Jamurtas AZ. Molecular etiology of exercise-induced inflammation. J Inflamm Res. 2016:175–86.
20. Fiala O, Hanzlova M, Borska L, Fiala Z, Holmannova D. Beyond physical exhaustion: Understanding overtraining syndrome through molecular mechanisms. Sports Med Health Sci. 2025; 7(4):237-48.
21. Gallo J, Raska M, Kriegova E, Goodman SB. Inflammation and its resolution in the musculoskeletal system. J Orthop Transl. 2017;10:52–67.
22. Greising SM, Corona BT, Call JA. Musculoskeletal regeneration following traumatic injury. Int J Sports Med. 2020;41(8):495–504.
23. Guo YT, Peng YC, Yen HY, Wu JC, Hou WH. Effects of probiotic supplementation on immune and inflammatory markers in athletes. Medicina (Kaunas). 2022;58(9):1188.
24. Gusev E, Zhuravleva Y. Inflammation: a new look at an old problem. Int J Mol Sci. 2022;23(9):4596.
25. Haller N, Behringer M, Reichel T, Wahl P, Simon P, Krüger K, et al. Blood-based biomarkers for managing workload in athletes. Sports Med. 2023;53(7):1315–33.
26. Haller N, Reichel T, Zimmer P, Behringer M, Wahl P, Stöggl T, et al. Blood-based biomarkers for workload management: emerging perspectives. Sports Med. 2023;53(11):2039–53.
27. Heaton LE, Davis JK, Rawson ES, Nuccio RP, Witard OC, Stein KW, et al. Selected in-season nutritional strategies to enhance recovery for team sport athletes. Sports Med. 2017;47(11):2201–18.
28. Herrero H. Sports and infections. In: Injury and health risk management in sports. Berlin: Springer; 2020. pp. 281–6.
29. Holgado D, Hopker J, Sanabria D, Zabala M. Analgesics and sport performance. PM R. 2018;10(1):72–82.
30. Hunter LE, Branch CA, Lipton ML. Neurobiological effects of repetitive head impacts in collision sports. Neurobiol Dis. 2019;123:122–6.
31. Izzy S, Grashow R, Radmanesh F, Chen P, Taylor H, Formisano R, et al. Long-term cardiovascular risk after traumatic brain injury. Lancet Neurol. 2023;22(10):959–70.
32. Jeukendrup AE, Areta JL, Van Genechten L, Langan-Evans C, Pedlar CR, Rodas G, et al. Does relative energy deficiency in sport exist? Sports Med. 2024;54(11):2793–816.

33. Kirsch D, Shah A, Dixon E, Kelley H, Cherry JD, Xia W, et al. Vascular injury and tau pathology in chronic traumatic encephalopathy. J Neuropathol Exp Neurol. 2023;82(2):127–39.
34. Langston PK, Mathis D. Immunological regulation of skeletal muscle adaptation to exercise. Cell Metab. 2024;36(6):1175–83.
35. Lee EC, Fragala MS, Kavouras SA, Queen RM, Pryor JL, Casa DJ. Biomarkers in sports and exercise. J Strength Cond Res. 2017;31(10):2920–37.
36. Lundberg TR, Howatson G. Analgesic and anti-inflammatory drugs in sports. Scand J Med Sci Sports. 2018;28(11):2252–62.
37. Małkowska P, Sawczuk M. Cytokines as biomarkers in exercise. Int J Mol Sci. 2023;24(13):11156.
38. Mavroudis I, Petridis F, Kazis D, Ionescu C, Novac B, Petroaie AD, et al. Traumatic brain injury and Alzheimer's disease overlap. Brain Broad Res Artif Intell Neurosci. 2025;16(2):7–18.
39. Meier TB, Huber DL, Goeckner BD, Gill JM, Pasquina P, Broglio SP, et al. Blood biomarkers of inflammation after concussion. Neurology. 2024;102(2):e207991.
40. Murray A, Cardinale M. Cold applications for recovery in adolescent athletes. Extreme Physiol Med. 2015;4(1):17.
41. Naughton M, Miller J, Slater GJ. Impact-induced muscle damage in contact sports. Int J Sports Physiol Perform. 2018;13(8):962–9.
42. Nieman DC, Mitmesser SH. Nutrition and immune recovery from heavy exertion. Nutrients. 2017;9(5):513.
43. Ortega E. Bioregulatory effect of exercise on innate immunity. J Physiol Biochem. 2016;72(2):361–9.
44. Punzi L, Galozzi P, Luisetto R, Favero M, Ramonda R, Oliviero F, et al. Post-traumatic arthritis and inflammation. RMD Open. 2016;2(2).
45. Recht GO, Lima-Cooper G, Buddenbaum CV, Sweeney SH, Bellini ZS, Newman SD, et al. Lifetime head impact exposure and inflammatory biomarkers. Neurotrauma Rep. 2025;6(1):638–50.
46. Ruchika FN, Shah S, Neupane D, Vijay R, Mehkri Y, Lucke-Wold B. Molecular progression of chronic traumatic encephalopathy. Int J Mol Sci. 2023;24(3):1847.
47. Saidi K, Abderrahman AB, Laher I, Hackney AC, Hage RE, Saeidi A, et al. Immune inflammation markers during congested match play. Sci Rep. 2024;14(1):30312.
48. Schwellnus M, Soligard T, Alonso JM, Bahr R, Clarsen B, Dijkstra HP, et al. IOC consensus on load and illness risk. Br J Sports Med. 2016;50(17):1043–52.
49. Silva FOC, Macedo DV. Exercise, inflammation and adaptation. Rev Bras Cineantropom Desempenho Hum. 2011;13:320–8.
50. Slattery K, Bentley D, Coutts AJ. Oxidative and inflammatory responses to training. Sports Med. 2015;45(4):453–71.
51. Sohail MU, Al-Mansoori L, Al-Jaber H, Georgakopoulos C, Donati F, Botrè F, et al. Cytokine and oxidative stress profiles in elite athletes. Front Physiol. 2020;11:600888.
52. Soriano S, Curry K, Sadrameli SS, Wang Q, Nute M, Reeves E, et al. Gut microbiome alterations after sport-related concussion. Brain Behav Immun Health. 2022;21:100438.
53. Stokes KA, Jones B, Bennett M, Close GL, Gill N, Hull JH, et al. Returning to play after prolonged training restrictions. Int J Sports Med. 2020;41(13):895–911.
54. Tabor JB, Brett BL, Nelson L, Meier T, Penner LC, Mayer AR, et al. Biomarkers of neurobiological recovery after concussion. Br J Sports Med. 2023;57(12):789–97.
55. Tarnowski M, Tomasiak P, Tkacz M, Zgutka K, Piotrowska K. Epigenetic alterations in sports-related injuries. Genes (Basel). 2022;13(8):1471.
56. van Amerongen S, Pulukuri SV, Tuz-Zahra F, Tripodis Y, Cherry JD, Bernick C, et al. Inflammatory biomarkers and neurobehavioral dysregulation in former football players. J Neuroinflammation. 2024;21(1):46.
57. VanItallie TB. Traumatic brain injury in collision sports and CTE. Metabolism. 2019;100:153943.
58. Varamenti E, Tod D, Pullinger SA. Redox homeostasis and inflammation in adolescent athletes. Sports Med Open. 2020;6(1):34.
59. Verduyn C, Bjerke M, Duerinck J, Engelborghs S, Peers K, Versijpt J, et al. Neurofilament levels in contact sport athletes. Neurology. 2021;96(15):705–15.
60. Walsh NP. Recommendations to maintain immune health in athletes. Eur J Sport Sci. 2018;18(6):820–31.
61. Walsh NP. Nutrition and athlete immune health. Sports Med. 2019;49(Suppl 2):153–68.
62. Waśkiewicz Z, Mukhambet Z, Azerbayev D, Bondarev S. Inflammatory response to ultramarathon running. Int J Mol Sci. 2025;26(13):6317.
63. Wegierska AE, Charitos IA, Topi S, Potenza MA, Montagnani M, Santacroce L. Physical exercise and gut microbiota. Sports Med. 2022;52(10):2355–69.
64. Zügel M, Maganaris CN, Wilke J, Jurkat-Rott K, Klingler W, Wearing SC, et al. Fascial tissue research in sports medicine. Br J Sports Med. 2018;52(23):1497.