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REGENERATIVE STRATEGIES FOR SPORTS-RELATED MUSCULOSKELETAL INJURIES: FROM PRP TO 3D BIOPRINTING

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ABSTRACT

Regenerative medicine is becoming an increasingly important part of sports medicine, especially in the treatment of musculoskeletal injuries that are difficult to manage with conventional methods alone. This review provides a structured and clinically focused overview of established and emerging regenerative therapies used in sports-related musculoskeletal conditions. Particular attention is given to platelet-rich plasma (PRP), mesenchymal stem cells (MSCs), exosome-based therapies, low-intensity pulsed ultrasound (LIPUS), hydrogel-based scaffolds, bone marrow aspirate concentrate, adipose-derived biologics, and three-dimensional (3D) bioprinting. A structured narrative review with scoping characteristics was conducted in accordance with PRISMA-ScR recommendations. Articles published between 2003 and 2025 were identified through PubMed, Scopus, Web of Science, and Google Scholar, with priority given to studies relevant to clinical practice, rehabilitation, functional outcomes, and athlete-centered recovery. The reviewed evidence suggests that PRP and MSC-based therapies currently represent the main biologic approaches in this field, while newer technologies offer promising but still largely experimental directions for future treatment. The value of regenerative therapies extends beyond tissue repair alone and may also influence rehabilitation, return-to-play, and quality of life. At the same time, their clinical use remains limited by methodological heterogeneity, lack of standardization, and insufficient long-term data. Further high-quality studies are needed to define clear indications, improve treatment protocols, and support the evidence-based integration of regenerative therapies into modern sports medicine.

KEYWORDS

Regenerative Medicine, Sports Injuries, Platelet-Rich Plasma, Mesenchymal Stem Cells, Rehabilitation, Return-to-Play

CITATION

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Introduction

Regenerative medicine has become an increasingly important part of modern sports medicine, especially in the treatment of musculoskeletal injuries that are difficult to manage with conventional approaches alone. This growing interest is linked to the fact that cartilage, tendons, ligaments, and osteochondral tissues often show limited healing capacity, particularly under conditions of repeated mechanical loading and early return to activity. In athletes and physically active individuals, treatment is expected not only to reduce symptoms, but also to restore function, support rehabilitation, and allow a safe return to sport (Caplan, 2007; Caplan & Correa, 2011; Shi & Gronthos, 2003).

Musculoskeletal injuries remain one of the main causes of pain, impaired performance, prolonged rehabilitation, and time lost from training and competition (Bahr & Krosshaug, 2005; Ekstrand et al., 2011; Finch, 2006). In many cases, standard treatment may improve symptoms, but it does not always restore tissue quality, mechanical function, or long-term durability of healing. This is particularly important in sports medicine, where incomplete recovery may lead not only to persistent symptoms, but also to recurrent injury, reduced confidence, and difficulty returning to previous performance levels.

For this reason, regenerative therapies are increasingly being studied as methods that may improve the biological environment of healing. Platelet-rich plasma (PRP) and mesenchymal stem cells (MSCs) are currently the most widely discussed approaches in this field. PRP is used mainly as a source of growth factors and biologic mediators that may support repair processes, while MSC-based therapies are of interest because of their immunomodulatory and paracrine effects on damaged tissue (Andia & Maffulli, 2017; Caplan & Correa, 2011; Gentile et al., 2017, 2020). At the same time, newer technologies such as exosome-based therapies, low-intensity pulsed ultrasound (LIPUS), hydrogel-based scaffolds, bone marrow aspirate concentrate, adipose-derived biologics, and three-dimensional (3D) bioprinting are expanding the regenerative treatment landscape and introducing more targeted and potentially more personalized strategies (Costa et al., 2025; Liu et al., 2024).

The importance of these therapies in sports medicine goes beyond structural healing alone. Their possible value also includes support of rehabilitation, reduction of symptom burden, improvement of functional recovery, and influence on return-to-play and quality of life. This broader perspective is important because athletes often experience not only physical limitations after injury, but also psychological stress, fear of reinjury, and uncertainty about return to sport (Ardern et al., 2013, 2016; Brewer et al., 2002; Filbay et al., 2016; Podlog & Eklund, 2007). As a result, the usefulness of regenerative medicine should be considered not only in biological terms, but also in relation to clinically meaningful outcomes.

At the same time, the current evidence remains heterogeneous. Regenerative therapies differ in composition, mechanism of action, degree of standardization, and level of clinical validation. Some methods, such as PRP, are already used in routine practice despite incomplete standardization, whereas others remain largely experimental. This makes careful interpretation necessary and highlights the need for structured reviews that connect biological rationale with practical clinical relevance.

Athletes represent a distinct group in regenerative medicine because intensive training and competition involve repeated mechanical loading, high metabolic demands, and accelerated tissue turnover (Chen et al., 2022; Kjaer, 2005; Magnusson et al., 2018). In this setting, many sports-related injuries develop not only as a result of a single traumatic event, but also because of cumulative microtrauma, repeated overload, and incomplete recovery between training sessions or competitions. Over time, this may impair endogenous healing, delay tissue repair, and increase the risk of chronic injury or reinjury (Ardern et al., 2016; Nyland et al., 2022). For this reason, athletes often require treatment strategies that support both biological healing and restoration of function under conditions of continued mechanical stress.

Within this context, regenerative therapies are of particular interest because they aim to improve the local healing environment rather than only reduce symptoms. PRP acts mainly through the release of growth factors that regulate inflammation, angiogenesis, and extracellular matrix remodeling (Andia & Maffulli, 2013; Dai et al., 2017). In athletes, these effects may be especially relevant during the early stages of recovery, when excessive inflammation can delay repair and when fibroblast activity, matrix synthesis, and controlled tissue remodeling are important for restoring structural integrity (Milano et al., 2010; Tang et al., 2024). This may help explain why PRP is often considered in conditions where early biologic support is expected to improve healing without the need for more invasive intervention.

MSCs promote tissue repair mainly through paracrine signaling rather than direct differentiation (Clarke et al., 2014; Henriksson et al., 2009; McIntyre et al., 2018). Their effect appears to depend largely on the release of cytokines and growth factors that can regulate inflammation, enhance vascularization, limit fibrosis,

and support resident progenitor cells. This may be particularly useful in athletes exposed to repetitive mechanical stress, where healing often requires not only structural repair but also restoration of a more favorable local biological environment (Molnar et al., 2022; Sonnet et al., 2010). In this sense, MSC-based therapies may be relevant not only in acute injury, but also in cases of incomplete recovery, recurrent symptoms, or progressive degeneration.

The relevance of regenerative medicine in athletes is also linked to the interaction between biological healing and mechanical loading. Tissue recovery in sports is never fully separate from rehabilitation, because repaired structures are gradually exposed to movement, strengthening, and sport-specific stress. Mechanical loading itself may influence regenerative signaling pathways, which means that the final clinical effect of biologic therapies may partly depend on how rehabilitation is planned and progressed (Nam et al., 2017; Sun et al., 2024). This may also apply to newer regenerative strategies, including exosome-based therapies, scaffold-supported repair, and other technologies designed to improve the local healing environment. As a result, the effect of regenerative treatment in athletic populations should be understood as part of a broader process in which biologic stimulation, tissue mechanics, and rehabilitation interact with each other.

For this reason, the mechanistic rationale for regenerative therapies in sports medicine is stronger when these methods are considered within the full context of recovery. In athletes, successful treatment depends not only on biological repair, but also on tissue durability, progressive loading tolerance, functional restoration, and safe return to sport. Regenerative therapies may help support these goals, but their effect is likely to depend on indication, timing, tissue type, and integration with a structured rehabilitation program.

Aim of the Review

This review aims to provide a structured, clinically focused overview of regenerative therapies for sports-related musculoskeletal injuries, with emphasis on PRP, MSCs, and emerging technologies, and to evaluate their relevance to rehabilitation, functional recovery, return-to-play, and quality of life in athletes (Riboh et al., 2016).

Materials and Methods

A structured narrative review with scoping characteristics was conducted in accordance with PRISMA-ScR recommendations (Tricco et al., 2018). Scientific articles published between 2003 and 2025 were identified through PubMed, Scopus, Web of Science, and Google Scholar using predefined keywords related to platelet-rich plasma, mesenchymal stem cells, regenerative medicine, sports injuries, exosomes, low-intensity pulsed ultrasound, bone marrow aspirate concentrate, adipose-derived biologics, hydrogels, tissue engineering, and three-dimensional bioprinting.

Original studies, systematic reviews, meta-analyses, and narrative reviews published in English or Polish were included. Case reports, conference abstracts, and studies lacking sufficient methodological transparency were excluded (Peters et al., 2015; Tricco et al., 2018). Priority was given to studies relevant to functional outcomes, rehabilitation, return-to-play, and clinical decision-making in sports medicine. The retrieved literature was analyzed qualitatively, with particular attention to mechanisms of action, treatment rationale, clinical indications, methodological consistency, and limitations of the current evidence base.

Platelet-Rich Plasma

Platelet-rich plasma (PRP) is an autologous blood-derived product obtained by centrifugation and characterized by an increased concentration of platelets and growth factors (Gentile et al., 2017, 2020). Its biological effect is mainly linked to platelet-derived molecules released from alpha granules, such as platelet-derived growth factor, vascular endothelial growth factor, fibroblast growth factor, transforming growth factor beta, epidermal growth factor, and insulin-like growth factor. These factors may support angiogenesis, cell proliferation, chemotaxis, and extracellular matrix synthesis, which explains the growing interest in PRP in musculoskeletal tissue repair (Andia & Maffulli, 2013; Blair & Flaumenhaft, 2009).

The clinical interest in PRP is based on the idea that tissue healing can be supported by concentrating natural biologic mediators already present in blood. In sports medicine, this is particularly attractive because many injuries involve tissues with limited healing capacity and are exposed to repeated mechanical stress. In athletes, the goal of treatment is not only tissue repair itself, but also restoration of function, reduction of symptoms, and safe return to training and competition. For this reason, PRP is often seen as a practical regenerative option that can be used in a minimally invasive way and integrated into broader treatment plans.

At the same time, PRP is not a single uniform product. Preparations may differ in centrifugation technique, platelet concentration, leukocyte content, activation method, and final volume, which makes studies difficult to compare and may partly explain differences in clinical outcomes (Dhurat & Sukesh, 2014; Gentile et al., 2020). Another important issue is the distinction between leukocyte-rich and leukocyte-poor PRP. These formulations may act differently depending on the treated tissue and clinical setting. In some cases, a higher leukocyte content may increase the inflammatory response, while in other situations a less inflammatory formulation may be more suitable. Although both activated and non-activated PRP show biological activity, the lack of standardization remains one of the main limitations of PRP in both research and clinical practice (Cavallo et al., 2016; Gentile et al., 2017).

This lack of standardization has practical consequences. If two studies use the same term, "PRP," but the final product differs in composition, dose, or method of administration, the results may not be directly comparable. This makes it difficult to define one optimal PRP protocol for all musculoskeletal conditions. It also explains why the literature sometimes shows promising results in one indication and much less convincing outcomes in another. In other words, the effect of PRP may depend not only on the diagnosis, but also on the exact formulation and the way it is used.

PRP has been studied in a range of sports-related conditions, including cartilage lesions, meniscal injuries, tendinopathies, ligament injuries, and early degenerative joint disease (Kon et al., 2011; Milano et al., 2010; Sun et al., 2010; Wei et al., 2012). This wide range of indications reflects both the biological versatility of PRP and the hope that it may improve healing in tissues that are difficult to treat with conventional approaches alone. In practice, however, its role appears to vary depending on the tissue type, severity of injury, and timing of treatment.

Particular attention has been given to knee osteoarthritis, where some studies suggest that PRP may provide better pain relief and functional improvement than hyaluronic acid, especially in earlier stages of disease (Cerza et al., 2012; Dai et al., 2017; Filardo et al., 2012; Tang et al., 2024). This is clinically relevant in active patients, because symptom control and better joint function may help maintain physical activity and delay more invasive treatment. At the same time, the published results are not fully consistent, and differences in patient selection, disease severity, PRP formulation, and follow-up duration may influence the observed benefit. This means that PRP may be useful in selected patients, but not necessarily in the same way across all cases of degenerative joint pathology.

PRP has also been investigated in tendon and ligament-related problems. The biological rationale for this is strong, because these tissues often show slow healing and poor vascularity. Growth factors contained in PRP may help stimulate local repair responses and improve the healing environment. Even so, the available evidence remains mixed, and not all studies report the same level of benefit. This may again reflect differences in pathology, chronicity of injury, injection protocol, and rehabilitation after treatment.

Another area of interest is anterior cruciate ligament (ACL) reconstruction. In this setting, PRP has been explored as an adjunct intended to support graft maturation and tendon-to-bone healing during early recovery (Cheng et al., 2010; Xie et al., 2013). The idea is biologically plausible, because improved local healing might in theory support graft integration and postoperative recovery. However, the clinical results remain inconsistent. Improvements seen in biological, imaging, or laboratory findings do not always translate into better function or better return-to-sport outcomes. This points to a broader issue in regenerative medicine research: surrogate markers of healing are not always the same as outcomes that matter most to athletes and clinicians.

This is especially important in sports medicine, where treatment success is rarely judged by imaging alone. Pain relief, strength recovery, functional stability, confidence in movement, and safe return to sport are often more meaningful than isolated biological markers. A therapy may appear promising from a mechanistic point of view, but still provide limited practical benefit if it does not improve rehabilitation or reduce reinjury risk. For that reason, PRP studies that focus only on biological healing may not fully answer the questions most relevant to everyday clinical practice.

PRP should also not be considered a stand-alone treatment. Its clinical value likely depends on the indication, timing of application, tissue type, and combination with appropriate rehabilitation. Biological support alone is unlikely to replace well-planned loading strategies, neuromuscular recovery, and careful return-to-play decisions. In athletes, this point is particularly important, because early symptom improvement may create pressure for rapid return even when tissue healing is still incomplete. PRP may therefore be most useful when integrated into a broader treatment strategy that combines biologic support with individualized rehabilitation and functional monitoring.

PRP remains one of the most accessible and widely used regenerative approaches in sports medicine. Its autologous nature and relatively simple preparation make it attractive in clinical practice. At the same time, differences between formulations and inconsistent results mean that its effects should be interpreted with caution. The current evidence suggests that PRP may be helpful in selected musculoskeletal conditions, but it should not be seen as a universal solution. More high-quality studies are needed to determine which patients, indications, and PRP protocols are most likely to provide meaningful clinical benefit.

Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) are multipotent stromal cells that can differentiate into connective tissue lineages, including chondrocytes and osteoblasts (Caplan, 2007; Orozco et al., 2011). Their clinical effect is thought to depend mainly on paracrine activity rather than direct differentiation. MSCs release cytokines and growth factors that can regulate inflammation, limit fibrosis, promote angiogenesis, and support resident progenitor cells (Caplan & Correa, 2011; Clarke et al., 2014; McIntyre et al., 2018). For this reason, MSCs are often discussed not simply as replacement cells, but as biologic regulators of the healing environment.

This point is important in sports medicine, because many musculoskeletal injuries do not fail to heal only because of tissue loss. In many cases, the local environment is also unfavorable, with persistent inflammation, poor matrix organization, and incomplete repair. MSC-based therapies are of interest because they may help modify this local environment in a way that supports recovery. In other words, their possible role is not limited to building new tissue directly, but also includes improving the conditions in which healing takes place.

In clinical practice, MSC-based therapies are mostly considered in conditions with more advanced tissue damage or in cases where conventional treatment does not restore satisfactory function. This includes degenerative joint disease, focal cartilage defects, and intervertebral disc pathology (Gupta et al., 2016; Henriksson et al., 2009; Orozco et al., 2011). These are situations in which standard conservative or procedural treatments may reduce symptoms, but do not always lead to full biological repair or long-term functional stability. This is why MSCs are often seen as a more advanced regenerative option, especially in difficult or chronic cases.

A major source of variability is the origin of the cells. MSCs can be obtained from different tissues, including bone marrow and adipose tissue, and this may influence their biological properties and clinical performance. Studies also differ in cell preparation, dose, route of administration, and treatment protocol. Because of this, the available evidence is difficult to compare and remains heterogeneous. This variability is one of the main reasons why the clinical literature on MSCs is still difficult to interpret in a consistent way.

The source of the cells may matter because not all MSC products behave in the same way. Cells derived from different tissues may differ in proliferative potential, signaling profile, and regenerative capacity. At the same time, most published studies are relatively small and use different processing methods, which makes it difficult to determine whether one source is clearly superior to another. As a result, even when studies report improvement, it is not always possible to identify which part of the treatment was responsible for the effect.

In knee osteoarthritis, meta-analyses suggest that MSC injections may improve pain and functional outcomes in selected patients (Gupta et al., 2016; McIntyre et al., 2018). These findings are encouraging, especially in active individuals, but the evidence is still limited by small study groups, differences in methodology, and inconsistent outcome measures. This makes firm clinical conclusions difficult. It also means that the positive results seen in some studies should be interpreted with caution, particularly when trying to apply them to athletes or highly active patients.

Another important point is that improvement in pain or function does not always mean that long-term tissue restoration has been achieved. In regenerative medicine, short-term symptom relief and biological repair are not always the same thing. This is especially relevant in sports medicine, where treatment decisions are often influenced by the pressure to return to training and competition. A therapy may appear successful in the short term, while its long-term effect on tissue durability, reinjury risk, or performance remains unclear.

In athletes, MSC-based therapies may be considered in recurrent injuries, persistent symptoms, or progressive degeneration when standard treatment fails to restore function and stability (Riboh et al., 2016). At present, their role in sports medicine is still developing. The biological rationale is strong, but the clinical evidence is not yet as established as in the case of more commonly used approaches such as PRP. This means that MSCs are often viewed as promising, but still selective therapies rather than routine options for everyday sports injury management.

Their use is also associated with practical and regulatory challenges, including cell sourcing, processing, storage, cost, and standardization. These issues are more complex than in simpler biologic therapies and may limit routine use in many clinical settings. In addition, the regulatory framework around cell-based treatment is often stricter, which may further restrict broad clinical application. For this reason, even though MSC-based therapies are biologically attractive, their translation into routine sports medicine remains slower and more complicated.

MSCs should also not be seen as isolated solutions. Their value is likely to depend on proper indication, timing, method of delivery, and integration with rehabilitation. Biological treatment alone is unlikely to restore full function if it is not supported by progressive loading, neuromuscular recovery, and careful monitoring of return to sport. This is particularly relevant in athletic populations, where the final goal is not only symptom improvement, but durable recovery and safe return to performance.

Taken together, MSC-based therapies represent one of the most promising areas of regenerative medicine. Their potential to influence inflammation, vascularization, and local tissue repair makes them relevant to musculoskeletal conditions that are difficult to treat with standard methods alone. At the same time, their current use should still be approached with caution, especially in routine clinical practice. More well-designed studies are needed to define their role, identify the most appropriate indications, and determine how they should be combined with rehabilitation in athletic populations.

Innovative Regenerative Therapies

In addition to established biologic approaches such as PRP and MSC-based therapies, sports medicine is increasingly exploring newer regenerative methods. The main reason is that many musculoskeletal injuries, especially those involving cartilage, tendons, ligaments, and osteochondral tissue, heal slowly and often incompletely. Standard treatment may reduce pain and improve function, but it does not always restore tissue structure, mechanical properties, or long-term performance. For this reason, newer regenerative therapies are being developed to support healing in a more targeted and, in some cases, more individualized way. Among the most promising are exosome-based therapies, low-intensity pulsed ultrasound (LIPUS), hydrogel-based scaffolds, bone marrow aspirate concentrate (BMAC), adipose-derived biologics, and three-dimensional (3D) bioprinting (Costa et al., 2025).

Exosome-Based Therapies

Exosomes are very small vesicles released by cells. They carry proteins, lipids, messenger RNA, and microRNA, which help cells communicate with each other. In regenerative medicine, the greatest interest is in exosomes derived from mesenchymal stem cells because these may reduce inflammation, support angiogenesis, and promote tissue repair (Tan et al., 2024; Zhang et al., 2025). Their action does not depend on replacing damaged tissue directly. Instead, they seem to improve the local biological environment and help surrounding cells respond to injury more effectively. Recent reviews also note that exosome source and cargo strongly affect therapeutic performance, which is one reason the field is moving toward more precise, engineered exosome products.

This is particularly relevant in sports medicine because tendon, ligament, cartilage, and rotator cuff injuries often heal slowly and incompletely. Experimental studies suggest that exosomes may improve matrix repair, reduce inflammatory damage, and support better tissue organization in these structures (Huang et al., 2020; Zhang et al., 2023). Another reason they are considered promising is that they may preserve some of the beneficial signaling effects of stem cells without the need to transplant living cells. They may also be easier to store and deliver than cell-based products.

At the same time, their clinical use remains limited by several problems. Studies differ in how exosomes are isolated, purified, measured, and delivered. Their content may vary depending on the source cells and the way they are produced. Because of this, results are difficult to compare and most positive findings still come from preclinical studies rather than routine clinical practice. This means that exosomes are promising, but they still require stronger standardization and better human studies.

Low-Intensity Pulsed Ultrasound

LIPUS is a non-invasive method that uses low-intensity ultrasound waves to stimulate biological processes involved in tissue healing. It does not deliver cells or biologic material into the lesion. Instead, it acts through mechanical stimulation of signaling pathways that may reduce inflammation, support cartilage repair, and promote chondrogenic differentiation (Chen et al., 2023). In simple terms, it is meant to activate healing through biophysical stimulation rather than through injection.

This makes LIPUS interesting in sports medicine because recovery after injury depends not only on tissue healing, but also on rehabilitation and gradual return to loading. LIPUS may therefore work best as a supportive method during recovery, especially in conditions where healing is slow and where progressive loading must be carefully controlled. Its possible advantage is that it can be combined with rehabilitation rather than replace it.

The main limitation is that the evidence remains inconsistent. Studies differ in treatment settings, treatment duration, timing of application, and target conditions. Because of this, it is still difficult to define which patients benefit most, when treatment should start, and how LIPUS should be combined with rehabilitation or other regenerative therapies. This means that its biological rationale is interesting, but its clinical role is still not clearly defined.

Hydrogel-Based Scaffolds

Hydrogels are advanced biomaterials that can act as supportive scaffolds for tissue repair. Their purpose is to create a local environment that helps cells survive, organize, and regenerate tissue more effectively. Many hydrogels are designed to mimic some of the physical and biochemical properties of native extracellular matrix, which may improve tissue integration and healing (Kang et al., 2024; Hashemi-Afzal et al., 2024). They can also be used as carriers for cells, growth factors, or extracellular vesicles. For this reason, they are often seen as active parts of a regenerative strategy rather than as simple fillers.

This is especially important in cartilage and osteochondral injuries, where natural healing is poor and the tissue later needs to tolerate high mechanical stress. Hydrogels may improve local repair conditions and help keep regenerative factors in the injured area for a longer time. This makes them attractive in cartilage engineering and in combined scaffold-based repair. Recent reviews describe them as one of the most promising support technologies in regenerative orthopedics.

Still, there are important limitations. A scaffold that works well in laboratory conditions may not perform equally well inside a joint exposed to repeated loading. Problems may include poor integration with host tissue, uncertain long-term durability, and difficulty translating laboratory designs into routine treatment. So while hydrogels are promising, they still need stronger long-term validation before they can be widely used.

Bone Marrow Aspirate Concentrate and Adipose-Derived Biologics

BMAC and adipose-derived biologics are often described as intermediate options between simple blood-based biologics and more advanced cell-based therapies. BMAC contains a mixture of nucleated cells, growth factors, cytokines, and progenitor cells obtained from bone marrow aspirate. Adipose-derived biologics are based on material obtained from adipose tissue and are considered attractive because this source is relatively accessible (Costa et al., 2025). These approaches are of interest because they may support healing through several biological pathways simultaneously rather than through a single isolated mechanism.

This broader biological activity may be particularly useful in cases where standard treatment does not lead to adequate tissue recovery. These methods are also closer to current orthopedic practice than some of the more futuristic technologies. Their main limitation, however, is variability. Product composition differs widely between preparations, protocols remain inconsistent, and the exact active component is often unclear. As a result, it remains difficult to compare studies and determine which patients are most likely to benefit (Costa et al., 2025).

3D Bioprinting

Three-dimensional bioprinting is one of the most advanced regenerative technologies currently under development. Its aim is to create a patient-specific construct that closely replicates the architecture and mechanical properties of native tissue. This is achieved by combining biomaterials, living cells, and bioactive molecules within a controlled spatial arrangement. The goal is not simply to fill a defect, but to recreate tissue in a more organized and functional way.

This approach is particularly promising in cartilage and osteochondral injuries, where tissue structure is complex and standard repair methods often fail to restore it adequately. In sports medicine, this is especially relevant because many injured tissues must later tolerate high functional loads. A scaffold that more closely matches the injured site may therefore improve the quality of reconstruction and, in the future, support more personalized treatment. This is one of the reasons why 3D bioprinting is often regarded as a future direction in sports orthopedics and regenerative medicine.

However, the challenges remain substantial. Major barriers include scaffold integration, vascularization, long-term mechanical durability, manufacturing complexity, cost, and regulatory approval. Most available evidence still comes from experimental research. This means that although 3D bioprinting is highly promising, it should currently be viewed as a future-oriented strategy rather than a method ready for routine clinical use.

General Perspective

Taken together, these emerging approaches show that regenerative medicine is moving toward more precise, combined, and potentially more personalized treatment strategies. Some methods, such as BMAC and adipose-derived biologics, are already closer to clinical application, whereas others, including exosomes, advanced hydrogels, and 3D bioprinting, remain more firmly within the area of translational research. Their future role in sports medicine will depend on whether promising biological mechanisms can be translated into clear clinical benefit, reproducible treatment protocols, and outcomes that are meaningful to athletes, including functional recovery, return to play, tissue quality, and long-term durability of healing. At the same time, these methods are associated with important limitations, including incomplete standardization, uncertain long-term outcomes, high cost, and the risk of premature or excessive use before strong evidence is available. For this reason, they should currently be regarded as promising developments rather than replacements for careful clinical judgment, structured rehabilitation, and evidence-based treatment planning.

Implications for Rehabilitation, Return-to-Play, and Athlete Quality of Life

In athletes, the value of regenerative therapies extends beyond tissue healing alone. Their potential role also includes support during rehabilitation, improvement of functional recovery, and possible influence on the timing and quality of return to sport (Ardern et al., 2013; Brewer et al., 2002; Podlog & Eklund, 2007). This is particularly important in sports medicine, where successful treatment is defined not only by structural repair, but also by restoration of performance, confidence, and everyday functioning.

Sports injuries often affect more than the injured tissue itself. Prolonged rehabilitation may be physically demanding, but it can also impose a considerable psychological burden on the athlete. Studies have shown that injured athletes may experience stress, anxiety, fear of reinjury, frustration, and uncertainty about returning to sport, all of which may negatively influence recovery and reduce quality of life (Ardern et al., 2011; Filbay et al., 2016; Forsdyke et al., 2016). In this context, treatment strategies that reduce pain and support recovery may also indirectly improve motivation and adherence to rehabilitation.

Regenerative therapies may be useful at this stage because they can support tissue repair and, in some cases, facilitate earlier functional progression. This may be particularly relevant in athletes, who often seek to return to training and competition as soon as possible. At the same time, faster symptom improvement should not be equated with complete healing. Reduced pain and improved short-term function do not necessarily indicate full biological recovery of the injured tissue. For this reason, return-to-play decisions should not be based solely on symptom relief, as this may increase the risk of reinjury (Ardern et al., 2016; van der Horst et al., 2017).

A safe return to sport requires a broader perspective. Biological healing should be considered alongside strength recovery, joint stability, neuromuscular control, progressive loading, and sport-specific readiness. Psychological factors are also important. Even when physical healing appears satisfactory, fear of reinjury or reduced confidence may delay return to sport or impair performance after return (Ardern et al., 2016; Forsdyke et al., 2016).

For this reason, regenerative therapies should be viewed as one component of a broader rehabilitation process rather than as isolated interventions. Their greatest value is likely to emerge when they are combined with structured rehabilitation programs that account for tissue recovery, functional progression, and psychological readiness. In practice, this means that biologic treatment should support rehabilitation, not replace it.

From an athlete-centered perspective, the main goal is not simply healing of the injured structure, but safe return to activity, reduced risk of recurrence, and preservation of quality of life. Regenerative medicine may contribute to these outcomes, but its role should always be interpreted within the broader context of rehabilitation and long-term recovery (Ardern et al., 2016; Forsdyke et al., 2016; van der Horst et al., 2017).

Discussion

The available evidence suggests that regenerative medicine is becoming an increasingly relevant part of the treatment of sports-related musculoskeletal injuries, particularly when conventional approaches do not lead to satisfactory recovery. PRP and MSC-based therapies remain the most widely discussed biologic strategies, whereas newer approaches such as exosome-based therapies, LIPUS, hydrogel-based scaffolds, BMAC, adipose-derived biologics, and 3D bioprinting reflect the next stage of development in this field. Although these methods differ in mechanism, level of evidence, and degree of clinical implementation, they share a common goal: to improve tissue healing and support recovery in a more targeted and biologically informed way.

Among currently available regenerative options, PRP appears to be the most accessible and the most widely used in routine clinical practice. Its popularity likely stems from its autologous origin, relatively simple preparation, and broad range of proposed indications (Gentile et al., 2017, 2020). At the same time, one of the main limitations of PRP is the lack of standardization. Variations in platelet concentration, leukocyte content, activation method, injection technique, and treatment schedule make it difficult to compare studies and identify which formulation is most appropriate for a given condition (Cavallo et al., 2016; Dhurat & Sukesh, 2014; Gentile et al., 2020). This may partly explain why PRP shows encouraging results in some settings, such as early knee osteoarthritis, while findings remain inconsistent in others (Cerza et al., 2012; Dai et al., 2017; Filardo et al., 2012; Tang et al., 2024).

MSC-based therapies may offer a broader biologic effect, primarily through paracrine signaling and modulation of the local healing environment rather than direct tissue replacement (Caplan & Correa, 2011; Clarke et al., 2014; McIntyre et al., 2018). This makes them particularly attractive in more complex clinical situations, such as degenerative joint disease, recurrent injury, or cases in which conventional treatment has failed to restore adequate function (Gupta et al., 2016; Riboh et al., 2016). However, the evidence remains difficult to interpret because studies vary substantially in cell source, dose, preparation method, delivery technique, and follow-up design. As with PRP, biologic promise does not necessarily translate into clear clinical recommendations. For this reason, MSC-based therapies remain promising, but are not yet fully established in routine sports medicine practice.

The newer methods discussed in this review show that regenerative medicine is gradually moving beyond simple blood-derived or cell-based products. Exosome-based therapies are of interest because they may retain some of the beneficial signaling effects of MSCs without requiring direct cell transplantation, and may promote tissue repair through anti-inflammatory and pro-regenerative mechanisms (Huang et al., 2020; Zhang et al., 2023). LIPUS represents a different strategy, as it aims to enhance repair through physical stimulation of biologic pathways rather than injection-based treatment (Chen et al., 2023). Hydrogel-based scaffolds and 3D bioprinting extend this concept further by combining biologic stimulation with structural support and elements of tissue engineering (Hashemi-Afzal et al., 2024; Kang et al., 2024; Liu et al., 2024; Xu et al., 2013). BMAC and adipose-derived biologics occupy an intermediate position, as they are closer to current orthopedic practice but still limited by major issues related to standardization and evidence quality (Costa et al., 2025).

These developments are important because they show that regenerative treatment is no longer confined to a single type of intervention. Instead, the field is expanding toward approaches that may influence healing through signaling pathways, mechanical stimulation, biomaterial support, or combined tissue-engineering strategies. This shift is particularly relevant in sports medicine, where injured tissues must often recover under high biomechanical demand, and where treatment success depends not only on symptom relief, but also on durable restoration of function.

A major challenge across nearly all regenerative therapies is the quality and consistency of the available evidence. Many studies differ in design, patient selection, treatment protocols, follow-up duration, and outcome measures. In some cases, biologic or imaging improvements are reported without clear gains in function, return-to-play, or reinjury rates. This creates a gap between biologic plausibility and clinical usefulness. In sports medicine, that gap is especially important because athletes and clinicians are usually more concerned with outcomes that affect real performance, recovery time, and long-term durability than with surrogate healing markers alone.

Another important issue is that regenerative therapies are often discussed in broad terms, even though their effects are likely to depend on the specific tissue being treated. A therapy that may be useful in a degenerative joint condition may not produce the same effect in tendon, ligament, or cartilage injury. This tissue-specific dimension is especially relevant for PRP and MSCs, but it also applies to newer technologies.

Exosomes, biomaterial scaffolds, and bioprinted constructs may ultimately need to be tailored to the biological and mechanical demands of a specific tissue rather than applied as universal regenerative tools.

The role of rehabilitation should also be emphasized. Regenerative therapies should not be viewed as stand-alone solutions. Their clinical value depends not only on the biologic product or technology itself, but also on timing, indication, rehabilitation quality, loading strategy, and follow-up. A treatment that appears promising in theory may provide limited benefit if used in the wrong clinical setting or without a structured rehabilitation program. This is particularly relevant in athletes, in whom early symptom improvement may create pressure for rapid return to sport even when tissue healing remains incomplete.

An athlete-centered perspective is therefore essential. In sports medicine, successful treatment means more than structural repair. It also includes restoration of function, confidence in movement, psychological readiness, and the ability to return to sport without an excessive risk of reinjury (Ardern et al., 2013, 2016; Brewer et al., 2002; Filbay et al., 2016; Podlog & Eklund, 2007). From this perspective, regenerative medicine should not be judged solely by imaging findings or laboratory markers, but also by outcomes such as rehabilitation burden, return to performance, recurrence risk, and quality of life. These measures may ultimately determine whether a regenerative therapy is truly useful in athletic populations.

From a practical standpoint, current evidence suggests that regenerative therapies should be used selectively and as part of a broader clinical strategy rather than as isolated interventions. PRP appears to be the most accessible option and may be considered in selected musculoskeletal conditions, especially when the aim is to support healing and reduce symptoms through a relatively low-risk, minimally invasive approach. MSC-based therapies may offer broader biologic potential, but their clinical use remains more complex because of limited standardization, regulatory constraints, and variable evidence quality. Newer approaches such as exosomes, hydrogels, and 3D bioprinting are scientifically promising, but at present they should be regarded mainly as emerging or translational strategies rather than routine therapeutic tools. In athletes, the decision to use regenerative treatment should therefore depend not only on biologic rationale, but also on injury type, stage of healing, rehabilitation planning, expected functional demands, and the risk of returning to sport before full biologic recovery has occurred.

The findings of this review suggest that regenerative medicine for sports injuries is currently developing rapidly, but the field has not yet reached full methodological or clinical maturity. Some therapies, particularly PRP, are already widely used despite incomplete standardization. Others, such as MSC-based treatments, remain more selective and clinically complex. The newest technologies are still largely confined to experimental or translational settings. In other words, the field is advancing faster than the evidence is becoming stable, which increases the risk that clinical enthusiasm may outpace the strength of the data.

This review also has several limitations that should be acknowledged. First, it was designed as a structured narrative review with scoping characteristics rather than a fully systematic review. Although the literature search was broad and focused on recent, clinically relevant evidence, the included studies were heterogeneous in design, patient populations, treatment protocols, and reported outcomes. This limits direct comparison between studies and makes it difficult to draw firm conclusions regarding the relative value of individual regenerative approaches. In addition, some of the newer strategies discussed in this review, such as exosome-based therapies, advanced hydrogel systems, and 3D bioprinting, are still supported mainly by preclinical or early translational evidence. For this reason, the conclusions of the present review should be interpreted as an overview of current directions and clinical potential rather than as definitive guidance for routine practice.

Future progress in this area will depend on better study design, clearer treatment protocols, and more consistent reporting of clinically relevant outcomes. Greater methodological consistency would improve comparability between studies and help identify which therapies are useful, in which patients, and at what stage of recovery. It will also be important to integrate biologic treatment more closely with rehabilitation planning rather than evaluating these components separately. For newer methods such as exosomes, hydrogels, and 3D bioprinting, future work will also need to address manufacturing quality, regulatory approval, long-term safety, and cost-effectiveness before these technologies can enter broader clinical use.

Taken together, the current evidence supports the growing role of regenerative medicine in sports-related musculoskeletal injuries, but it also highlights clear limitations. PRP and MSC-based therapies currently have the strongest clinical relevance, whereas exosome-based therapies, LIPUS, hydrogel-based systems, BMAC, adipose-derived biologics, and 3D bioprinting represent promising but less established directions. Their future place in sports medicine will depend on whether these approaches can move from encouraging biologic concepts to clear, reproducible, and athlete-centered clinical benefit.

Summary and Conclusions

Regenerative medicine is becoming an increasingly important part of the management of sports-related musculoskeletal injuries, particularly in cases where conventional treatment does not provide complete recovery. PRP and MSC-based therapies remain the main biologic approaches in this field, while newer strategies such as exosome-based therapies, low-intensity pulsed ultrasound, hydrogel-based scaffolds, bone marrow aspirate concentrate, adipose-derived biologics, and 3D bioprinting are broadening the future therapeutic landscape (Caplan, 2007; Caplan & Correa, 2011; Costa et al., 2025; Riboh et al., 2016; Shi & Gronthos, 2003).

The potential value of these therapies extends beyond tissue repair alone. In sports medicine, their relevance also includes possible effects on rehabilitation, functional recovery, return to play, and quality of life (Ardern et al., 2013, 2016; Brewer et al., 2002; Filbay et al., 2016; Podlog & Eklund, 2007). At the same time, the current evidence is limited by variability in treatment protocols, lack of standardization, and inconsistent reporting of outcomes. These factors make direct comparison difficult and require cautious interpretation of published findings.

At present, PRP appears to be the most accessible and widely used regenerative option, whereas MSC-based therapies remain biologically promising but more complex in terms of standardization and clinical application. Newer technologies offer interesting future possibilities, particularly in more targeted and personalized treatment, but most of them are still at an early stage of clinical development (Hashemi-Afzal et al., 2024; Huang et al., 2020; Liu et al., 2024; Xu et al., 2013).

Future research should focus on high-quality clinical studies with stronger methodological consistency and greater emphasis on outcomes that are directly relevant to athletes. This includes not only pain relief or imaging findings, but also return to performance, risk of reinjury, rehabilitation burden, and long-term recovery. With stronger evidence and better integration into rehabilitation planning, regenerative therapies may become a more reliable component of evidence-based sports medicine practice.

Overall, the future role of regenerative medicine in sports injuries will depend not only on biologic efficacy, but also on whether these therapies can be integrated into structured rehabilitation pathways and translated into outcomes that matter to athletes. In this context, quality of return to play, risk of reinjury, long-term function, and quality of life may be just as important as tissue repair itself. Regenerative strategies should therefore be understood not as stand-alone solutions, but as components of a broader, individualized, and athlete-centered treatment model.

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