The 2020 NBA Orthobiologics Consensus Statement

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This 2020 NBA Orthobiologics Consensus Statement provides a concise summary of available literature and practical clinical guidelines for team physicians and players. We recognize that orthobiologic injections are a generally safe treatment modality with a significant potential to reduce pain and expedite early return to play in specific musculoskeletal injuries. The use of orthobiologics in sports medicine to safely reduce time loss and reinjury is of considerable interest, especially as it relates to the potential effect on a professional athlete. While these novel substances have potential to enhance healing and regeneration of injured tissues, there is a lack of robust data to support their regular use at this time. There are no absolutes when considering the implementation of orthobiologics, and unbiased clinical judgment with an emphasis on player safety should always prevail. Current best evidence supports the following:

Key Points

There is support for the use of leukocyte-poor platelet-rich plasma in the treatment of knee osteoarthritis.

There is support for consideration of using leukocyte-rich platelet-rich plasma for patellar tendinopathy.

The efficacy of using mesenchymal stromal cell injections in the management of joint and soft tissue injuries remains unproven at this time. There are very few data to suggest that current cell therapy treatments lead to any true functional tissue regeneration. Meticulous and sterile preparation guidelines must be followed to minimize the risk for infection and adverse events if these treatments are pursued.

Given the high variability in orthobiologic formulations, team physicians must stay up-to-date with the most recent peer-reviewed literature and orthobiologic preparation protocols for specific injuries.

Evidence-based treatment algorithms are necessary to identify the optimal orthobiologic formulations for specific tissues and injuries in athletes.

Changes in the regulatory environment and improved standardization are required given the exponential increase in utilization as novel techniques and substances are introduced into clinical practice.

Keywords: NBA; National Basketball Association; orthobiologics; consensus statement; PRP; BMAC

Techniques and approaches to improve the biologic aspects of tissue healing hold great promise for treatment of soft tissue and articular cartilage injuries in athletes. These "orthobiologic" agents encompass a variety of injectable substances, including isolated growth factors, platelet-rich plasma (PRP) and other autologous blood formulations, and cell therapy approaches using cells derived from bone marrow, properly prepared and preserved amniotic sources, or adipose tissue. Preclinical studies have demonstrated a strong potential for enhanced tissue healing in the presence of orthobiologics, sparking great enthusiasm among researchers, physicians, and patients worldwide.

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The underlying rationale for their clinical use in professional athletes is that optimization of the local biologic environment can potentially promote healing of tissues with otherwise limited inherent healing capacity, such as cartilage, muscle, tendon, ligament, and meniscus.[108] Many clinical trials have been initiated under the assumption that promising results obtained by preclinical studies would translate into a meaningful clinical effect in professional athletes. Although preliminary results of some studies have suggested that orthobiologics may play a role in the management of musculoskeletal injuries in athletes, allowing earlier return to play, decreased pain, and lower injury recurrence rate,[4,21,77] other studies have not found similar results.[27,59,105,106] Overall, there is currently very little high-quality evidence to support the use of orthobiologics in sports medicine.

It is critical to distinguish which orthobiologic preparations are effective and safe for the management of a specific

injury to identify the optimal treatment options, provide realistic expectations, and minimize the risk for adverse events. Adherence to appropriate indications and meticulous preparation protocols is key to achieving superior outcomes.[108] This consensus statement provides a concise summary of currently available orthobiologic treatment options and serves as a practical resource when considering the use of orthobiologics in common musculoskeletal injuries seen in National Basketball Association (NBA) players. Tantamount to efficacy, athlete safety remains the primary principle to which we must adhere when contemplating the role of these still evolving and often unproven alternatives.

METHODS

The NBA research committee (members include 8 orthopaedic surgeons and 1 primary care sports medicine physician) convened to outline the goals and process required for an evidence-based consensus statement regarding the use of orthobiologics for the management of common musculoskeletal injuries in NBA players. PubMed, Embase, and Google Scholar databases were searched in January 2020 for studies presenting outcomes of orthobiologics for the management of preselected common injuries in professional basketball players. Relevant articles were concisely summarized to present the NBA research committee representatives with the most up-to-date literature. A consensus statement was drafted, revised, and approved by the NBA research committee, NBA team physicians executive committee (members include 4 orthopaedic surgeons, 1 primary care sports medicine physician, and 1 internal medicine physician), and the National Basketball Players Association.

CURRENTLY AVAILABLE ORTHOBIOLOGICS

Platelet-Rich Plasma

PRP is perhaps the most widely used orthobiologic therapy for the management of musculoskeletal injuries in athletes. PRP is a relatively safe preparation that is produced using a sample of the patient's own blood. The sample undergoes centrifugation that allows concentration of platelets in a small volume of plasma.[148] PRP also contains an abundance of proteins that may potentially decrease inflammation, reduce pain, and expedite recovery from soft tissue injuries.[11,49,78,84,88,108,111] However, high-quality clinical evidence to support the use of PRP in specific musculoskeletal injuries in professional basketball players is limited. Moreover, studies are heterogeneous in terms of indications, PRP formulation protocols, dosing, delivery method, and more.[15,42,116,128] The lack of standardization hinders the ability to aggregate available data and therefore precludes development of concrete, evidence-based treatment algorithms for the use of PRP for most acute and chronic cartilage or soft tissue injuries.

Cell-Based Therapies ("Stem Cells")

The concept of using stem cells to augment tissue healing has received much attention in recent years owing to the potential to heal and even regenerate tissues. Stem cells are defined by their self-renewal ability and inherent plasticity, which allows differentiation into many different cell types based on the biologic environment to which they are exposed.[104,109] While embryonic stem cells are truly pluripotent and can differentiate into all 3 primary germ layers, multipotent adult stem cells harbor the potential to differentiate into 1 germ layer only (eg, mesenchymal stromal cells may differentiate into bone, tendon, cartilage, or muscle).[31,104] Preclinical studies have suggested that stem cells can potentially promote angiogenesis and tissue regeneration in addition to harboring immunomodulatory and anti-inflammatory effects.[¶] Current data suggest that the primary mechanism for the positive effects of stem cells is via paracrine effects, whereby the cells modulate the local environment to promote healing and repair, rather than direct participation in tissue regeneration. Although stem cell therapy harbors tremendous potential for improved and expedited tissue healing, high-quality evidence to support its use in injuries in NBA players is not available at this time.[108]

At present, stem cells can be procured from autologous bone marrow, autologous adipose tissue, or allogenic amniotic tissue. Although bone marrow and adipose tissue do contain a small number of stem cells as defined by currently accepted cellular and molecular criteria, the current

[¶]References 17, 34, 40, 58, 86, 113, 117, 130, 142, 145.

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regulatory environment in the United States does not allow isolation and subsequent culture expansion of this small number of cells. As a consequence, it is critically important to recognize that the number of true stem cells by formal criteria in currently available preparations is very small. Furthermore, the number of live cells surviving the harvesting, processing, and manufacturing procedures in allogeneic preparations, such as amniotic tissues, remains unknown. In fact, leading investigators have suggested that the term "connective tissue progenitors" should be used rather than "stem cells" to recognize the more limited biologic activity of the cell formulations in current use.[92] Several countries other than the United States permit cell culturing to increase the number of available cells, leading some patients to seek these treatment overseas via "medical tourism." Patients electing to do so should be cautious, as in many cases, the standards for cell processing and manufacturing are unknown and often less stringent as in the United States. Research endeavors in this decade will attempt to identify the optimal harvesting, processing, and delivery techniques of stem cells for the management of specific injuries in athletes. Further studies are crucial to identify the composition and biologic activity of different cell therapy formulations. Efforts to standardize and regulate protocols worldwide may aid in achieving the mutual goal of improving patient care and minimizing the risk for adverse events.[28,67,90,91,100]

SAFETY AND ADVERSE EVENTS

The currently available and US Food and Drug Administration–approved orthobiologics are considered relatively safe, and serious adverse events are rare. Autologous orthobiologic preparations, such as PRP and bone marrow aspirate concentrate (BMAC), are inherently safe, and concerns regarding transmittable diseases or major immunogenic reactions associated with allograft or xenograft preparations have been virtually eliminated.[3] However, minor immunogenic reactions have been reported with the use of PRP injections, and the presence of bovine thrombin in PRP preparation kits can theoretically cause an antibody-mediated coagulopathy.[3] A relatively common adverse effect of PRP injections is a local inflammatory response, including pain, swelling, and local skin reaction,[50] which is self-limited and does not require treatment in most cases. Patients should be informed that although rare, infections have been reported with the use of PRP injections.[104]

Cell-based therapies may carry risks related to tissue harvesting, processing, and delivery. Risks associated with harvesting include complications related to bone marrow aspiration, such as infection, serious bleeding, or breakage of the needle. These adverse events are rare, with an estimated adverse event rate of 0.07%.[6,64] Handling of any tissue outside of the patient's body is associated with some risk of infection, and severe, albeit rare, infections have been reported with the use of autologous and allogenic orthobiologics.[109] This reflects the critical importance of seeking these treatments from responsible providers using US Food and Drug Administration–approved protocols, with meticulous handling and processing of materials that are safest for the athletes.

MANAGEMENT OF SPECIFIC PATHOLOGIES

A summary of the 2020 NBA Orthobiologics Consensus Statement recommendations for the management of specific musculoskeletal injuries is presented in Table 1.

Knee Cartilage Injury

Focal knee cartilage injuries are a common cause of pain and disability in athletes. The limited ability of cartilage tissue to regenerate after injury can ultimately result in significant time lost from play, early-onset osteoarthritis, and a shortened professional athletic career.[36,38,47,112]

There is currently no high-quality evidence to support the use of orthobiologic injections alone for the treatment of focal knee cartilage injury. Several studies have shown promising results with the use of PRP or BMAC as an *adjunct* to surgical treatment of focal cartilage defects.[16,76,93] Current data suggest that such positive effects are likely due to anti-inflammatory activity of the cells rather than true tissue healing or regeneration ("symptom modifying" rather than "structure modifying"). The role of orthobiologic injections in the conservative management of articular cartilage defects of the knee is currently under investigation and requires further rigorous study.[76,122] Data to date have suggested a potential role for symptomatic relief, but improved tissue regeneration is entirely unknown and is not supported by currently available published clinical studies.

Knee Osteoarthritis

Acute chondral injuries of the knee may draw more attention in active NBA players, owing to fear of requiring emergent surgical intervention and significant time lost from play. However, management and possible prevention of knee osteoarthritis are also of great importance to the aging athlete.

Leukocyte-poor PRP (LP-PRP) formulations and mesenchymal stromal cell injections have been shown to be effective for relieving symptoms of knee osteoarthritis. The ability of these injections to reverse or halt progression of osteoarthritis is not supported at this time.[#] Although most studies have not specifically focused on athletes, younger patients with less severe osteoarthritis seem to achieve greater relief of symptoms using PRP injections.[22,74] At this time, it seems that LP-PRP may be superior to leukocyte-rich PRP (LR-PRP) for knee osteoarthritis.[107] However, high-quality studies directly comparing the 2 have yet to be published. More recently, the efficacy of using hyaluronic acid–PRP conjugates in the management of knee osteoarthritis has been investigated. While preliminary outcomes of hyaluronic acid–PRP conjugates are encouraging, evidence is still limited.[51]

[#] References 14, 22, 25, 37, 39, 45, 48, 54, 74, 81, 98, 126, 135.

TABLE 1
Summary of the 2020 NBA Orthobiologics Consensus Statement Recommendations[a]

Injury	Recommendation
Focal cartilage injury of the knee	At this point, the NBA Team Physicians Society and the NBPA recognize the lack of sufficient evidence to support the use of orthobiologic injections for the definitive treatment of focal cartilage defects of the knee, although their use may be considered a safe yet unproven alternative for symptom modification in the absence of tissue repair.
Knee osteoarthritis	• PRP, BMAC, and adipose-derived mesenchymal stromal cells can be safely used for symptomatic relief in an NBA player with evidence of knee osteoarthritis. Of these, LP-PRP has the most supportive evidence at this time. • The player should be counseled that prevention of osteoarthritis progression is unlikely with these injections and that prospects for tissue regeneration are doubtful at this time.
Myotendinous injury	The NBA Team Physicians Society and the NBPA do not recommend the routine use of orthobiologic injections for acute muscle injuries at this time.
Patellar tendinopathy	• The NBA Team Physicians Society and the NBPA recommend the use of PRP injections (preferably LR-PRP) for the management of patellar tendinopathy in NBA players as an adjunct to first-line conservative treatment and/or when conservative measures fail. • At this point, the NBA Team Physicians Society and the NBPA recognize the lack of sufficient evidence to recommend the use of cell-based therapy for patellar tendinopathy.
Ankle sprains	• The NBA Team Physicians Society and the NBPA recommend considering on a case-by-case basis LP-PRP injection for the management of high-ankle sprains. • The NBA Team Physicians Society and the NBPA do not recommend the use of orthobiologic injections for low-ankle sprains at this time.
Achilles tendinopathy	The NBA Team Physicians Society and the NBPA do not recommend the use of orthobiologic injections for Achilles tendinopathy at this time.
Plantar fasciopathy	• The NBA Team Physicians Society and the NBPA recommend consideration of the use of PRP injections for the management of plantar fasciopathy in NBA players as an adjunct to first-line conservative treatment and/or when conservative measures fail. • At this point, the NBA Team Physicians Society and the NBPA recognize the lack of sufficient evidence to support the use of cell-based therapy for plantar fasciopathy and cannot therefore recommend its routine use.
Surgical augmentation	• At this time, there is no evidence to support the use of PRP to augment ACL reconstruction and/or meniscal repair. • BMAC and adipose-derived stromal vascular fraction cells may be additive in cartilage restoration procedures, yet we cannot recommend the routine use based on existing data.

[a]ACL, anterior cruciate ligament; BMAC, bone marrow aspirate concentrate; LP-PRP, leukocyte-poor platelet-rich plasma; LR-PRP, leukocyte-rich platelet-rich plasma; NBA, National Basketball Association; NBPA, National Basketball Players Association; PRP, platelet-rich plasma.

Several clinical studies have evaluated the efficacy of using adipose-derived mesenchymal stromal cells and BMAC injections for knee osteoarthritis. Most of these uncontrolled studies have reported good to excellent improvement in patient-reported outcomes, particularly in patients with mild to moderate osteoarthritis.[13,16,62,66,72,76] However, a randomized comparison of BMAC and placebo injections for bilateral knee osteoarthritis showed no difference in improvement in pain between the groups.[121]

Myotendinous Injury

Muscle injuries are extremely common in basketball players, and while mild injuries may not even be reported by the athlete, severe muscle tears may result in significant time lost from play and muscle weakness and predispose the player to injury recurrence. Orthobiologics are currently being evaluated for their ability not just to accelerate rehabilitation and shorten the duration of player disability but also to improve the structural integrity of the healing muscle to minimize atrophy and weakness and to decrease the risk of recurrent injury.

The majority of research on using PRP injections for muscle injuries pertains to acute hamstring tears. The best available evidence does not support the use of PRP or mesenchymal stromal cell injections for acute muscle injuries in athletes.[**] Given the heterogeneity in terms of study design, injury type, and PRP formulation, the true potential of using PRP injections in the management of myotendinous injury remains largely unknown. Recently, the use of platelet-poor plasma (PPP) has been the subject of increasing interest among investigators and has shown promise for this application.[32,87] This is due to laboratory evidence demonstrating that the use of PPP or nonneutrophil–containing PRP subjected to an additional spin to remove platelets results in stimulation of myoblast differentiation, which is necessary for skeletal muscle regeneration.[87] However, at this time, clinical evidence regarding the use of PPP for myotendinous injuries is scarce.

Patellar Tendinopathy

Patellar tendinopathy, also referred to as "jumper's knee," is common in NBA players, presumably because of the repetitive explosive load to the extensor mechanism of the knee during jumping activities. Several studies have

**References 1, 8, 57, 59, 105, 106, 109, 143, 146.

reported significant relief of symptoms with the use of LR-PRP injections for the management of chronic patellar tendinopathy.[††] Of these, the studies with the best quality of evidence demonstrated improved outcomes using LR-PRP injections.[35,55] While most studies support the use of PRP in patellar tendinopathy, a recent level 1 study failed to show a significant difference in outcomes comparing LR-PRP, LP-PRP, and saline.[119]

Only a few studies have been published on the efficacy of using cell-based therapy for the management of patellar tendinopathy. The use of BMAC injection has been shown to provide significant improvement in outcomes for up to 5 years in a small sample of patients.[97]

Ankle Sprains

Ankle sprains are one of the most common injuries in professional basketball players.[20,63,85] Mild low-ankle sprains can usually be managed using the RICE protocol (rest, ice, compression, elevation) and physical therapy with minimal time lost from play. However, more severe low- and high-ankle sprains may result in significant time lost from play, and recurrence can be frequent.

Limited available evidence does not support the use of PRP in the management of low-ankle sprains. The data for high-ankle sprains are equivocal.[9,110] A case series of stable high-ankle sprains treated using LP-PRP injections reported earlier return to play and a faster decrease in pain.[79,114] We are unaware of high-quality clinical studies supporting the use of BMAC or other cell-based therapy in the management of ankle ligament injuries in professional athletes.

Achilles Tendinopathy

Achilles tendinopathy can present in escalating severity, ranging from minimal dull pain to a debilitating injury affecting performance and precluding play. Although a variety of conservative treatments have been developed, management of Achilles tendinopathy remains a challenge in many affected players.

Most studies have reported no significant role for using PRP or mesenchymal stromal cell injection for Achilles tendinopathy. A few high-quality studies have evaluated the efficacy of using PRP injections for the management of Achilles tendinopathy. Most studies found no improvement in outcomes with the use of PRP injections.[27,69,70,75,80] Of importance, 1 study found reduced tendon thickness after using PRP injections,[10] a finding that by itself may potentially reflect accelerated tendon remodeling. Evidence for the use of cell-based therapy for Achilles tendinopathy is limited[132] and insufficient to support concrete clinical recommendations.

Plantar Fasciopathy

The plantar fascia is prone to repetitive injury in NBA players because of the ballistic nature of motion required while jumping, running, cutting, and changing pace.[19,23,82,127] Injuries may present as an acute injury or rather a more gradual presentation of chronic pain accompanied by acute exacerbations.

Use of PRP may be considered for the management of refractory plantar fasciopathy as an adjunct to physical therapy in certain cases. There is some limited literature showing favorable outcomes with the use of PRP injections when compared with corticosteroids for plantar fasciopathy. Although PRP and corticosteroids facilitate improvement in outcomes, evidence has suggested a slightly greater improvement with the use of PRP and a lower complication rate.[‡‡] More large-scale, high-quality studies are warranted because of the heterogeneity, small sample sizes, relatively short follow-up periods, and lack of data regarding complications in most available studies.

A few randomized controlled trials have evaluated the efficacy of using amniotic-derived cell injections for the management of plantar fasciopathy.[12,61,147] The results of these studies are promising and suggest that amniotic-derived products may play a role in the management of pain attributed to plantar fasciopathy. Notably, current data indicate that there are few, if any, viable cells in currently available amniotic preparations.[96] At this time, no definite conclusions can be made because of the heterogeneous nature of the available limited data.

SURGICAL AUGMENTATION

Expedited return to play is a paramount concern for any athlete undergoing surgical intervention. Several studies have assessed the ability of different orthobiologic agents to enhance healing, decrease postoperative pain, and shorten the time of rehabilitation after orthopaedic procedures. Among these procedures are anterior cruciate ligament (ACL) repair,[52] ACL reconstruction,[§§] meniscal repair,[24,56,68,71,99,101] and treatment of chondral defects.[16,53,60,93] Some studies have found a beneficial effect of biologic augmentation of several surgical procedures with various orthobiologics.[7,16,52,53,68] However, evidence to support significant improvement in clinical outcomes and expedited return to play with the combination of orthobiologics and surgical procedures is limited. At this time, there are insufficient data to support the routine use of PRP to augment healing after ACL reconstruction, cartilage/meniscal repair, rotator cuff repair, or labral repair procedures.

SUMMARY KEY POINTS

This 2020 NBA Orthobiologics Consensus Statement may be used by team physicians as a resource when treating musculoskeletal injuries in NBA players. It is important to recognize that physicians will need to regularly review emerging literature in the context of this statement. In

[††]References 18, 35, 41, 46, 55, 73, 134, 138, 140, 141.

[‡‡]References 83, 89, 94, 102, 118, 123–125, 131, 133, 144.

[§§]References 2, 5, 7, 26, 29, 30, 33, 43, 44, 65, 95, 103, 115, 120, 129, 136, 137, 139.

addition, this statement will need periodic updates so that the conclusions remain current and timely.

While this consensus statement focuses on the use of orthobiologics in the management of musculoskeletal injuries in NBA players, it may likely also be applicable in part to other recreational and professional athletes and active individuals.

The literature to date provides the most support for the use of LP-PRP in the treatment of knee osteoarthritis and consideration of the use of LR-PRP for tendon pathology.

Given the high variability in orthobiologics formulations, we urge team physicians to stay up-to-date with the most recent literature and orthobiologic preparation protocols for specific injuries. Meticulous and sterile preparation guidelines must be followed to optimize outcomes and minimize the risk for adverse events.

Ongoing research will provide a deeper insight and understanding of the true merit of orthobiologics. Evidence-based treatment algorithms need to be developed to improve outcomes by identifying the optimal orthobiologic formulations for specific injuries in athletes. Changes in the regulatory environment and improved standardization will be required given the exponential increase in utilization as novel techniques and substances are introduced into clinical practice.

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