Articular Cartilage Damage and Knee Osteoarthritis in Athletes

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Outline

Learning Objectives

Following review of this material, the reader will:

1. Describe the prevalence of knee osteoarthritis in athletes;
2. Explain the cost implications of knee osteoarthritis in a younger patient population;
3. Describe the composition and function of articular cartilage;
4. List possible mechanisms of articular cartilage injury in athletes;
5. Compare and contrast various surgical and non-surgical techniques for articular cartilage repair;
6. Describe important components of rehabilitation for athletes with articular cartilage damage or post-surgical repair.

Articular Cartilage Damage and Knee Osteoarthritis in Athletes

Introduction

Osteoarthritis (OA) is a condition associated with damage to a joint's articular cartilage and leads to changes in underlying bone and joint margins.[1] OA may develop idiopathically, but most likely predisposing factors lead to development of the disease.[1] Metabolic disorders, anatomic derangements, major trauma, and inflammatory disease are well recognized causes of OA.[1] Athletes are particularly exposed to high-energy loading, cumulative joint stress, and excessive physical demands with little recovery time.[2] In addition, participation in contact or collision sports makes athletes susceptible to traumatic injury. Therefore, OA has been recognized as a potentially negative long-term health risk for former athletes.[2]

Osteoarthritis is prevalent in the general United States population with evidence suggesting that by 65 years of age almost all people have some OA in the hands and/or feet.[3] In addition, the Framingham Osteoarthritis Study reports that approximately 33% of survey participants between 63 to 93 years old had knee OA.[3] By the year 2020, it is estimated that almost 60 million Americans will be affected by arthritis.[3]

Athletes may be at a higher risk than the general population for developing OA. A retrospective cohort study examining former elite runners and tennis players found a 2 to 3 fold increase in radiographic hip and knee OA compared to age matched controls.[4] Additional literature reported male endurance, mixed, and power sport athletes had a greater chance of developing OA compared to age matched controls, with odds ratios calculated as 1.73, 1.90, and 2.17, respectively.[5] Athletes may also display signs and symptoms of arthritic changes earlier than the general population. Athletes may show development of OA 5 to 10 years after a sports related injury or as early as 30 to 40 years of age.[6,7] Additional research reports mixed sport athletes seeking medical care for OA at a mean age of 58.2 years old.[5] Moreover, 40% of retired NFL athletes who were surveyed reported development of OA

under the age of 60 years old.[8] Some authors have coined these people "the young patients with old knees".[9(p1759)]

Knee OA can greatly impact former athletes. Tibiofemoral and patellofemoral pain is associated with limitations in sports and recreational activities, increased difficulty in daily weight bearing activities, and diminished quality of life.[10] Economic burden of knee OA is also a concern. In Victoria, Australia $265 million was spent in the hospital treatment of sports related injuries, with an addition $110 million utilized to treat injuries to the lower limb.[6] As the number of people seeking treatment for sports related and lower extremity injuries continues to rise, there is concern for an increase in societal cost and greater burden to the healthcare system as more people are participating in sports, sustaining a sports related injury, and subsequently developing OA.[6]

Physical therapists frequently encounter patients with OA in a variety of practice settings. As sports participation and injuries continue to occur, clinicians should be aware of the prevalence and impact of OA in an athletic population. In addition, it is important to understand the structure and function of articular cartilage (AC), potential mechanisms of injury leading to OA, and conservative and surgical management of the condition to serve this unique patient population and promote the best possible outcomes.

Articular Cartilage

Structure. OA is associated with damage to AC, which leads to exposure and harm of the underlying bone.[1] Therefore, it is critical for clinicians to understand AC structure and how it is influenced by OA. In a healthy state, AC is mostly comprised of collagen, proteoglycans, and water; there are very few chondrocytes, and a non-existent blood, neural, and lymphatic supply.[11,12] Type II collagen provides protection from tensile and shear stress, while the proteoglycans' protein structure maintains the AC matrix.[12] Glycosaminoglycans (GAGs) are covalently bonded to the proteoglycans.[12]

Water is a major component of AC, and water's interaction with the solid matrix is critical for the maintenance of the tissue's mechanical properties. It is thought that GAGs play an integral part in maintaining the fluidity of the tissue through the presence of a negative charge.[13] The negative charge attracts positive ions in the fluid matrix, such as sodium and calcium, creating osmotic pressure in the tissue.[13] As AC is loaded, water is moved through the extracellular matrix, allowing for fluid support of external loads; then, as the tissue is unloaded, fluid is able to return to the structure.[13] Ultimately, frictional resistance against fluid flow is very high, causing tissue permeability to be low; in addition, the pressure of the fluid matrix allows for the tissue to withstand significant loading.[12]

In addition to its composition, AC is typically classified into zones and regions (Appendix A). The superficial zone contains parallel collagen fibers, as well as flattened chondrocytes.[12] The superficial zone protects underlying layers and resists shear, tensile, and compressive forces.[12] Deep to the superficial zone is the middle zone, which is responsible for most of the AC volume.[12] Collagen is more randomly organized in the middle zone compared to the superficial layer with fewer chondrocytes.[12] Deep to the middle zone is the deep zone, which resists most compressive forces due to the high proteoglycan content; collagen is arranged perpendicularly, allowing for better attachment to the underlying bone.[12]

Regionally, AC is organized into pericellular, territorial, and interterritorial matrices, which surround chondrocytes in the tissue. The pericellular region is adjacent to the cell membrane and mostly consists of proteoglycans.[12] The territorial matrix surrounds the pericellular matrix and is composed of collagen.[12] This region is thought to assist in load bearing. Finally, the interterritorial region is large with randomly oriented collagen fibers and an abundance of proteoglycans.[12]

AC has limited healing capability when damaged by a traumatic mechanism or degenerative disease, such as OA. There are multiple factors that limit healing, including the presence of very few chondrocytes and limited blood supply.[11,12] Typically when AC is damaged, type I collagen infiltrates the

area instead of type II collagen; this diminishes the tissue's resilience and stiffness.[14] Moreover, proteoglycan and GAG content diminishes with OA; water is less able to bind to the tissue, which consequently brings more water into the area.[13] Though more water is surrounding the tissue, bonding ability continues to be diminished causing a more solid matrix to carry external mechanical loads.[12,13] This leads to greater AC stiffness and subsequently more damage to the subchondral bone.

Function. The unique structure of AC allows the tissue to complete a variety of functions. The main purposes of AC are to provide a low friction articulation and to facilitate the transmission of loads to the underlying bone.[12] The interaction between the solid phase and fluid phase of the tissue is responsible for its abilities to provide a low friction surface and transmit forces.[12] As force is applied through mechanical loading, fluid pressure increases in the tissue and allows fluid to flow out of the extracellular matrix. The movement of fluid creates a large frictional drag and prevents excessive amounts of fluid from leaving the matrix too quickly.[12] In addition to the fluid dynamics of the tissue, the behavior of the collagen and proteoglycan matrix allows for significant load support and appropriate transmission of forces to subchondral bone.[12]

OA disrupts the structure of AC and prevents normal interaction between the solid phase and fluid phase of the tissue. Damage decreases the ability of the tissue to deform and allows fluid to flow quickly out of the extracellular matrix when loaded; ultimately, this causes a great amount of pressure to the underlying bone leading to damage, pain, and decreased function.

Mechanisms of Articular Cartilage Injury in Athletes

Athletes are particularly susceptible to injury due to repetitive loading, cumulative joint stress, and excessive physical demands. In addition, participation in contact or collision sports makes athletes vulnerable to traumatic injuries. Injurious stressors associated with athletics leaves this unique population at risk to develop AC damage and OA, which can greatly limit a once active lifestyle.

Ligamentous injuries are common in athletics with the anterior cruciate ligament (ACL) being the most commonly disrupted knee ligament.[9] Typically, other musculoskeletal damage is associated with ACL rupture, including menisci, other ligaments, cartilage, and/or bone injury.[9] More than 100,000 ACL reconstructions occur annually in the United States, and research indicates that damage to the ACL can result in future AC damage.[9] The rate of OA 10 to 20 years post-ACL injury are widely reported between 10% to 90%.[9] Overall, AC is susceptible to injury after ligamentous damage because joint stability is compromised; an increase in anterior tibial translation and internal tibial rotation occurs. Greater contact stresses arise in the posterior medial and lateral compartments, as well as frictional abrasion which promotes the breakdown of tissue.[15] A retrospective study by Lohmander et al examines the prevalence of knee OA in female soccer players 12 years after an ACL rupture.[16] There were 103 female soccer players with a mean age of 31 years that participated in the study.[16] Of those that consented to radiographs, 82% had visible changes and 51% were considered to have knee OA using the Kellgren-Lawrence scale.[16]

Meniscus injury, as well as subsequent removal or partial removal of the meniscus, can contribute to knee OA. The incidence of meniscus injury has been reported as much as 2.5-fold higher than ACL injury but frequently meniscal tears are missed or undertreated.[9] The meniscus has a variety of functions; mostly, it attenuates force and pressure throughout the knee joint. The meniscus may also act as a joint stabilizer; therefore, if the meniscus is injured or removed, AC is susceptible to increased pressure, greater forces, and possible injury. Meniscus lesions are associated with a high risk of cartilage loss with research reporting approximately 50% of individuals with previous meniscectomies having radiographic evidence of knee OA 15 to 20 years post-surgical intervention.[9] In addition, those that received an isolated meniscus resection scored significantly worse on the Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales of Sports and Recreation and Knee-Related Quality of Life 14 years post-surgical intervention compared to an age-matched reference group.[9]

Traumatic injury to knee AC cartilage leaves athletes susceptible to future OA. Contact and collision sports, such as soccer and football, often result in tackles that directly affect the knee joint. Injurious forces may damage AC of the knee with focal defects reported in up to two-thirds of patients undergoing knee arthroscopy.[14] Unfortunately, cartilage defects without proper surgical intervention results in poor healing, decreased resiliency of tissue, less stiffness, poor tissue characteristics, and possible future OA.[14]

The repetitive loading associated with excessive participation in sports is thought to increase the risk of developing knee OA because of cumulative AC microtrauma.[1] The development of OA is dependent on the amount, type, and intensity of sport with OA more commonly seen in track and field, as well as racket sports, compared to athletes that swim or cycle.[1] Sports with high impact loading with fast acceleration and deceleration have the highest relative risk for developing OA.[1] However, repetitive impact does not seem to be the only factor to blame for increased risk of OA; moreover, Lane et al published several studies suggesting that long distance running had no effect on development of OA or musculoskeletal disability.[17,18] Therefore, not only repetitive impact sports but physical characteristics and biomechanical factors, such as body weight and poor gait mechanics, should be considered as contributing factors to OA.[1]

Treatment Options

Surgical Repair to Protect AC. Ligamentous and meniscal repair is critical in order to protect AC following an athletic injury. The ACL is the most common knee ligamentous injury in athletics; in addition, ligamentous stability of the knee is critical to protect AC from damaging shear forces and frictional abrasion.[9] Therefore, ACL repair should occur as soon as possible after injury and diagnosis. A systematic review by Chalmers et al compared 27 cohorts that had undergone ACL reconstruction compared to 13 cohorts that were treated non-operatively.[19] At a mean 13.9 years after injury, those that had an ACL reconstruction had fewer meniscal injuries, less need for subsequent surgery, and

significantly improved activity level compared to those that did not receive surgery.[19] However, authors reported no significant differences in radiographic evidence of OA between the groups.[19] One possible limitation of this review was that ACL reconstruction occurred at a mean of 20.8 months after injury, which allows ample time for potential AC damage to occur. Krutsch et al recommends that ACL reconstruction occur within 6 months following injury to preserve the meniscus and reduce the risk of developing OA.[20]

A meniscal tear may occur independently or be associated with a concomitant injury, such as an ACL rupture. A review of the risk factors associated with the development of knee OA found that meniscal injury, including meniscectomy, meniscal tear, or meniscal surgery, was the most frequently reported factor associated with arthritic changes.[15] In addition, literature describes the importance of maintaining as much meniscal tissue as possible during surgery with greater likelihood of knee OA development in people post-total meniscectomy compared to those post-partial meniscectomy.[15] If possible, a meniscus repair should be performed in order to preserve tissue.[21] Mechanically, vertical mattress sutures provide stronger fixation compared to horizontal sutures, and repair techniques may be enhanced by fibrin clots, meniscal abrasion, platelet-rich plasma (PRP), or biomedical scaffolding.[21]

Surgical Repair of AC. Athletes with osteochondral lesions have poor cartilage healing and are susceptible to advancing arthritis; therefore, several surgical techniques have been developed to replicate hyaline cartilage and promote better outcomes in patients. Microfracture is considered the first line of treatment to promote blood flow to injured tissue. The microfracture procedure has shown promise with research indicating that 80% of patients improved in self report measures 7 years post-microfracture procedure.[14] However, the long term outcomes of the microfracture technique is questionable with a majority of the damaged tissue being replaced with fibrocartilage and less than 10% being replaced with hyaline cartilage.[14]

The osteochondral autograft transfer (OAT) technique harvests donor plugs from non-weight bearing areas to fill defects with mature, articular cartilage.[14] Good to excellent results were reported 10 years post-operatively in 90% of the patients who had the procedure to regain AC at the femoral condyle or tibial plateau. Unfortunately, poorer results are associated with lesions larger than 3 cm^2 (Appendix B). Autologous chondrocyte implantation (ACI) may be appropriate for larger lesions and involves the harvesting of chondrocytes from a non-weight bearing area.[22] Culture-expanded chondrocytes are placed in the area of defect and covered by a periosteal flap or collagen membrane.[22] Mithofer et al describes functional outcomes and return to soccer 4 years post-ACI procedure in 45 athletes.[23] Overall, 72% had good to excellent results based on the Brittberg knee rating scale but only 33% of athletes were able to return to competitive soccer.[23] Osteochondral allograft transplantation (OCA) is another option for large chondral lesion but chondrocyte viability is a concern which directly correlates to clinical success.[14] Success of transplantation has been reported at 82% at 10 years, 74% at 15 years, and 66% at 20 years.[14] Unfortunately, literature is limited regarding the outcomes of OCA in an athletic population.

A systematic review compared microfracture, OAT, and ACI procedures.[24] All techniques demonstrated improvement compared to pre-operative status. There was no clear benefit of ACI versus microfracture in short-term, but clinical outcomes diminished for the group receiving microfracture treatment after 2 years.[24] The OAT technique had a trend for better Lysholm scores compared to ACI; moreover, the OAT procedure produced a more rapid improvement in patients compared to ACI.[24] However, a defect size >4 cm^2 was predictive of better outcomes using ACI compared with other techniques (Appendix B).[24]

Murray et al summarizes several less common and newly developing procedures to restore damaged AC, including neocartilage implantation, cartilage autograft implantation system (CAIS), cartilage allograft implantation, and osteochondral graft substitutes.[22] Neocartilage implantation utilizes

autologous chondrocytes exposed to hydrostatic pressure on a 3-dimensional matrix to encourage production of AC; initial literature suggests the technique is safe and effective.[22] CAIS uses autologous cartilage implanted onto a scaffold; subjective patient scores and MRI evidence demonstrate positive results. Cartilage allograft implantation uses allograft chondrocytes in fibrin glue, while the osteochondral graft substitute utilizes an implant to match the layers of cartilage and subchondral bone; unfortunately, there is limited evidence to support the use of these techniques. [22]

For athletes that sustained ligamentous, meniscal, and/or traumatic cartilage damage while participating in sports, a total knee arthroplasty (TKA) may be necessary several years post-injury to treat the pain and functional deficits associated with OA. Moreover, the risk of knee OA and subsequent knee arthroplasty was significantly greater for former elite athletes compared to matched controls, with former athletes reporting significantly more knee injuries as well.[25] Unfortunately, patients are often counseled to delay a knee replacement as long as possible to decrease the need for possible revisions[26]; for former athletes, who may present with OA younger than the general population, activity modification, loss of strength, decrease of functional ability, and poor quality of life might occur. Therefore, conservative management options must be considered for this unique patient population before undergoing a TKA.

Non-Surgical Options. Growth factors including PRP and bone marrow aspirate concentrate (BMAC) may be useful to repair chondral lesions when an osteochondral autograft is not an option secondary to unusual defect size or location.[22] PRP has been shown to enhance tissue regeneration, decrease pain, and improve patient reported outcomes in subjects with chondral lesions and OA for up to 6 months, while BMAC has shown promising improvements in AC repair of animal models.[22,27]

Patients may also opt for hyaluronic acid injections which are thought to supplement synovial fluid that has become less viscous, as well as promote cartilage matrix synthesis.[28] A systematic review by Aggarwal and Sempowski evaluated the effectiveness of hyaluronic acid injections for knee OA. [28]

Results demonstrated significant improvements in pain, activity level, and function with hyaluronic acid injections, with most improvements noted after 12 weeks.[28] However, the minimally significant changes are not thought to be clinically beneficially by the American Academy of Orthopedic Surgeons (AAOS).[22] Corticosteroid injections, which are thought to decrease the inflammatory process associated with OA, have also been shown to reduce pain and improve patient global self-assessment.[29] A systematic review summarized by Law et al determined that steroid injections have beneficial effects that last for about 1-4 weeks.[29] However, corticosteroids should be used with caution because of collagen degradation associated with use.[29]

Mesenchymal stem cell implantation is showing promising results for AC regeneration. Stem cells may be isolated from bone marrow, adipose tissue, and umbilical cord tissue and used to signal chondrogenesis.[30] A cohort study by Kim et al examined the effects of implanted versus injected stem cells in patients with knee OA.[31] Both International Knee Documentation Committee (IKDC) scores and Tegner activity scores improved significantly in both groups; however, cartilage repair was significantly better in the implantation group compared to the injection group when using the International Cartilage Repair Society grading system.[31]

Glucosamine is a nutritional supplement that is commonly used in patients with mild arthritic changes to improve symptoms and decrease cartilage degradation.[32] Results are mixed about the product's effectiveness; a review of treatment agents by Gallagher et al reported 1500 mg of glucosamine daily significantly decreased the loss of joint space width compared to a placebo control group.[33] Conversely, a review by Kongtharvonskul et al reported no beneficial effects of glucosamine in regards to joint space narrowing, but did report improved function and decreased pain using the Western Ontario and McMaster Universities Arthritis Index (WOMAC).[32]

Finally, pulsed electromagnetic field therapy is a viable adjunct to surgical intervention and has been reported to increase proteoglycan synthesis and decrease inflammation.[22] However, parameters of

the therapy reported in the literature included use for 6 hours per day for 90 days, which might be difficult for patients to follow.[34]

Rehabilitation

Preventative strategies should be adopted by athletes at risk for developing knee OA, either due to previous injury or the repetitive impact associated with sports. It is recommended that physical therapists counsel athletic patients to diversify training regimens by incorporating low impact activities, such as cycling and swimming.[22] Further interventions, such as shock absorbing insoles, wedge insoles, and variable-stiffness sole shoes, have been shown to decrease joint loading.[35] Use of a prophylactic knee brace may be beneficial in providing joint stability; however, literature explains that knee braces typically cannot resist large forces that are placed on the knee during high-intensity sports.[1] In addition, incorporating a structured warm-up routine before practice or competition may be beneficial in reducing future injury in athletes of all ages and activity levels, regardless of history of previous injury.[22]

For rehabilitation of an athlete post-ACL and/or meniscal repair, return to sport will be a top priority. Generally, meniscus repair will require 8 to 12 weeks of recovery, while an ACL repair may take 6 to 12 months before return to sport activities. To reduce the risk of OA, return to sport should be a gradual, controlled process with emphasis on restoring muscular strength, power, endurance, flexibility, and proprioception.[1] Rehabilitation following chondral repair is typically even more intensive. Average time to return to sport for OAT, microfracture, or ACI procedures range from 6.5 to 7 months, 8 to 17 months, and 18 to 25 months, respectively.[22] In addition, research reports a wide range of successful returns; between 33% to 96% of athletes retuning after an ACI, 59% to 66% after a microfracture, and 91% to 93% after an OAT procedure.[22] The OAT technique allows for early loading, while the ACI procedure does not allow for early weight bearing as the graft adheres to subchondral bone.[22] Overall, rehabilitation should consist of a progression beginning with protection and joint activation, moving to joint loading and return to function, and concluding with activities to mimic sport specific demands.[22]

Physical therapists should assist athletes in correcting malalignments, which may contribute to musculoskeletal injury and AC damage due to excessive contact pressures. Knee OA typically develops in the medial compartment due to the high internal contact forces from an external knee adduction moment during gait.[36] Research indicates that using a lateral wedge shifts the mechanical axis of the limb and decreases contact pressure.[36] Moreover, pronation, knee valgus, hip internal rotation, and adduction during vigorous sporting activities leave athletes susceptible to ACL and meniscus injury, which could precede knee OA.[35] Orthotics, bracing, and/or a neuromuscular control exercise program may be beneficial for a patient that presents with this pattern.[35]

Therapists may also target an athlete's muscle strength if weakness, particularly of the quadriceps muscle is a concern. Evidence suggests that quadriceps weakness, especially in women, could increase the risk of developing knee OA.[35] In addition, research suggests that knee extensor strength is a protective factor against symptoms of knee OA when comparing subjects with low adjusted isokinetic knee extensor strength to those with high isokinetic extensor strength.[35]

Conclusion

Ultimately, athletes are at a higher risk for developing knee OA secondary to repetitive impact, high-intensity loading, and/or history of a traumatic injury. Damage to AC and development of knee OA can decrease quality of life and greatly diminish the activity level of this unique population. Physical therapists may serve an integral role in managing athletic injuries, initiating post-operative rehabilitation, and helping current or previous athletes return to a high level of function. Therefore, it is imperative for therapists to recognize the important structural and functional aspects of AC, possible mechanisms of injury to the tissue, surgical and non-surgical repair options, and evidence based rehabilitation techniques. By integrating this information into practice, physical therapists can promote the best possible outcomes in a unique, athletic patient population.

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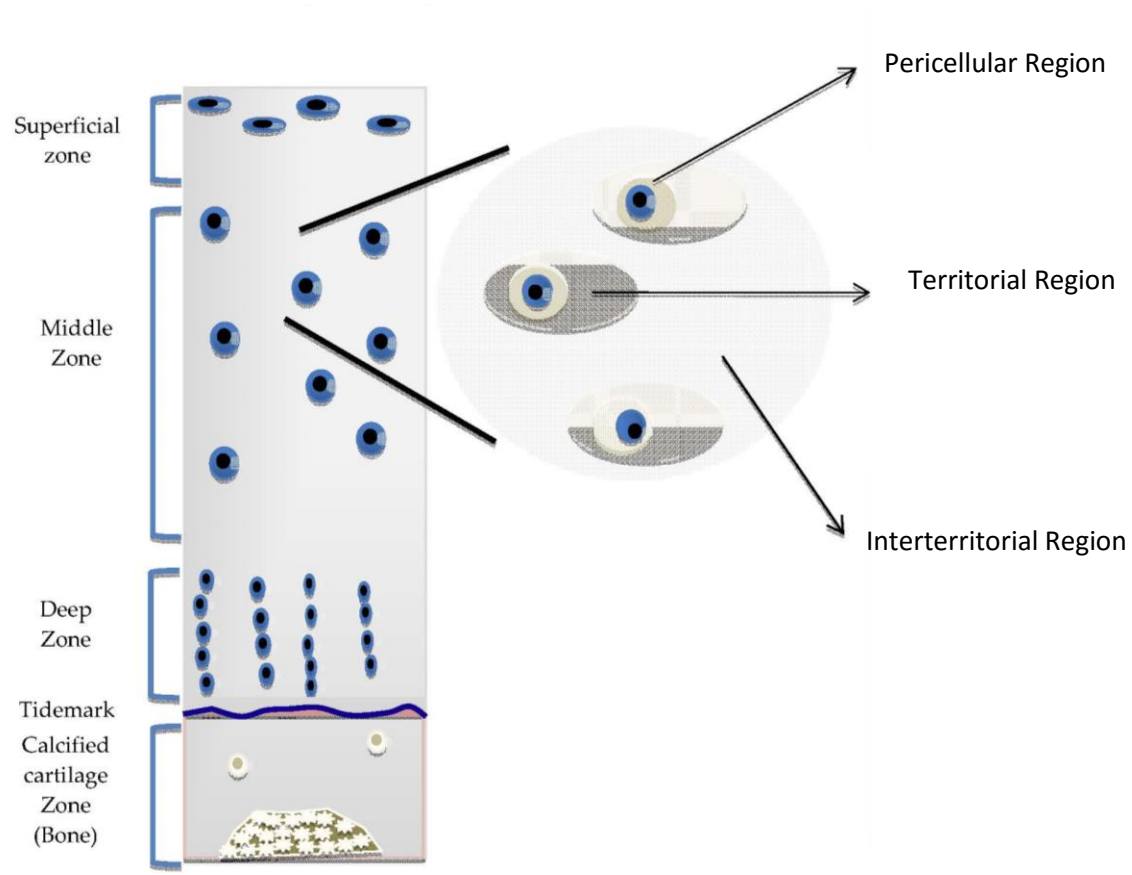
Appendix A: Articular Cartilage (AC) Zones and Regions[37]



Pictorial description of AC organization into zones and regions. A tidemark is present between the final zone and calcified layer of tissue. (Source: García-Carvajal et al in *The role of extracellular matrix (ECM) and novel strategies, regenerative medicine and tissue engineering*.)

Appendix B: Surgical Procedure Indication Based on Lesion Size[14]

Lesion Size, cm^2	Indicated Procedure
<2	Microfracture OAT
2-4	OAT ACI
>4	ACI OCA

Evidence based recommendations for surgical intervention of AC damage based on size of lesion. OAT= osteochondral autograft transfer; ACI= autologous chondrocyte implantation; OCA=osteochondral allograft. (Source: Richter et al in *Knee Articular Cartilage Repair and Restoration Techniques*.)