Articular Cartilage Injury

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INTRODUCTION

- Articular cartilage is a complex structure lining the articulating surfaces of diarthrodial joints. It provides a smooth, low-friction surface, while minimizing peak stress on the underlying subchondral bone.
- Injuries to the chondral surfaces occur in all joints of the human body. Articular injury of the knee has received the most attention in the literature. This chapter will focus primarily on articular injury as it pertains to the knee joint; however, many of the principles of evaluation, grading, and management hold true for chondral injury in any anatomic joint.
- Injury to articular cartilage is very common; in one retrospective review of 31,516 knee arthroscopies, 63% of patients were found to have chondral injury (1). Cartilage injury of the knee affects approximately 900,000 Americans annually, resulting in over 200,000 surgical procedures (2). Notably, the literature analyzing the prevalence of articular cartilage pathology does not provide significant guidance or insight into the prevalence of lesions that are or become symptomatic and require treatment.
- Although nonsurgical management of articular cartilage injury has remained largely the same over the past decade, surgical treatment of chondral injuries continues to evolve. Reparative, restorative, and reconstructive techniques continue to be refined, giving surgeons more tools and options for biologic reconstruction of articular surfaces. In the last 2 decades, a decline in the volume of performed marrow stimulation techniques, such as microfracture, has occurred with a commensurate increase in more complex cartilage restoration procedures (3,4).

BASIC SCIENCE

- Articular cartilage is composed of water (65%–80% of wet weight), collagen (10%–20% of wet weight), proteoglycans (10%–15% of wet weight), and chondrocytes (5% of wet weight). The collagen in native cartilage is primarily type II, with smaller quantities of types V, VI, IX, X, and XI. Chondrocytes are the cells responsible for the production of the extracellular matrix. These cells differentiate from mesenchymal stem cells during skeletal morphogenesis and are subsequently a low turnover cell type. Chondrocytes receive their nutrition and oxygen from the surrounding synovial fluid via diffusion (5). In the intact, uninjured knee, the articular cartilage shares load-bearing responsibility with the menisci (up to 70% from the lateral meniscus), making the chondral surfaces significantly vulnerable to injury and degeneration with partial or complete injury or removal of the menisci.
- Four zones and the tidemark establish articular cartilage. Each zone is distinct and classified by the shape of the respective chondrocytes and the orientation of the type II cartilage. Superior to inferior, these zones are the superficial zone, intermediate zone, deep zone, tidemark, and calcified cartilage zone that lay above the subchondral bone. The superficial zone is composed of a high number of flattened chondrocytes and is packed tightly with collagen fibers aligned parallel to the surface. This structure aids in the protection and maintenance of the subsiding layers. Representing 40%–60% of the total cartilage volume, the intermediate zone provides resistance to compressive forces and is formed by a low density of spherical chondrocytes and thicker, more oblique layer of collagen. The third layer, the deep zone, is composed of vertical collagen fibrils, parallel columnar chondrocytes, and a high proteoglycan content that fulfill the role of providing the greatest resistance to impact. The tidemark is the distinguisher of the deep zone from the calcified layer. The chondrocytes here are hypertrophic and cell population is scarce (5,6).
- Cartilage being avascular, aneural, and alymphatic, relies heavily on diffusion for cell nutrition and waste removal. Chondrocyte division and migration is limited, resulting in the healing response being poor. Partial-thickness injury that does not penetrate the tidemark, the demarcation between the deep layer and calcified layer of cartilage, will result in cellular insult with decreased matrix production by the underlying and surrounding chondrocytes and ultimately little healing. In cartilage matrix and cell injuries, decreased proteoglycan concentration, increased hydration, and disorganization of the collagen network occur (1,5).
- Injury that penetrates the tidemark into the calcified cartilage layer and the subchondral bone (an osteochondral lesion)

will elicit an inflammatory response that includes an influx of marrow contents (undifferentiated mesenchymal stem cells, cytokines, and growth factors including transforming growth factor-β [TGF-β] and platelet-derived growth factor [PDGF]) triggered by hemorrhage and fibrin clot. The osteochondral injury has potential for a more robust healing response including a resultant repair that more closely resembles fibrocartilage, compared to native hyaline cartilage, and is composed of primarily type I collagen. This fibrocartilage-like repair is less stiff and more permeable than normal articular cartilage (1,5). Fibrocartilaginous repair tissue is far less durable than native hyaline cartilage and often begins to show evidence of depletion of proteoglycans, increased hydration, fragmentation and fibrillation, increased collagen content, and loss of chondrocytes within 1 year (7).

- Although the natural history of chondral injuries is not completely understood, it is postulated that defects, particularly larger, full-thickness injuries, can progress via edge loading and elevated contact pressures on the adjacent articular surfaces. This progression may lead to degradation of the surrounding chondral surfaces and ultimately osteoarthrosis. Symptoms of pain, swelling, stiffness, and locking or catching often accompany this progression that limits patient activities (8).

Patient Evaluation

- Articular cartilage injury can be caused by an acute injury that results in a focal chondral or osteochondral injury or chronic/subacute injuries or conditions that result in degenerative lesions. Damage to the chondral surfaces can occur in isolation or, as is often the case, in association with other intra-articular injury. The evaluating physician should maintain a high index of suspicion for chondral injury when evaluating the knee for any causes of pain, effusion, instability, or mechanical symptoms. Conversely, a comprehensive patient evaluation is paramount to establish a clear clinical correlation between imaging findings and a patient's symptoms, as a substantial number of focal chondral defects identified on imaging studies may be asymptomatic.
- A thorough history should include details related to the onset of symptoms (traumatic or insidious), mechanism of injury, previous injuries and surgery, and symptom-provoking activities. Importantly, symptoms from focal chondral defects within the knee must be distinguished from those of diffuse knee osteoarthritis, which often has a more severe presentation characterized by a dull, achy pain with recurrent knee swelling and pain when rising from a seated position (9).
- A thorough physical examination should evaluate formal alignment, abnormal gait, swelling, effusions, instability, meniscal symptoms, range of motion, strength, and neurovascular abnormalities. Crepitus, catching, locking, or grinding can occur with focal irregularities of the articular surfaces. Diagnosis of all concomitant pathology is critical to formulate a successful, global treatment plan.
- Radiographic workup should include posterior-anterior, weight-bearing, 45° plain films and patellofemoral, and non–weight-bearing lateral projections. Evaluation on plain films for joint space narrowing, subchondral sclerosis, osteophytes, and cysts should be performed. History and physical examination, along with these radiographs, are often all that is needed to make the appropriate diagnosis. Magnetic resonance imaging (MRI) can be valuable to assess the status of the knee ligaments and menisci but can underestimate the degree of cartilage abnormalities seen during arthroscopy (10). Use of 3.0-Tesla (T) magnets, cartilage imaging sequence techniques including fat-suppressed or fat-suppressed spoiled gradient-echo imaging, and balanced free precession steady-state sequences have improved detection and characterization of chondral injuries using MRI (11). Routine MRI sequences are typically sufficient to evaluate for subchondral abnormalities that may become useful findings during definitive decision making.

GRADING OF ARTICULAR CARTILAGE INJURY

- MRI provides excellent soft-tissue contrast and resolution for noninvasive evaluation of chondral injuries. MRI of cartilage is typically performed on high-field strength systems of at least 1.5 T, whereas 3 T systems are being increasingly used as well. Conventional MRI sequences can be used to detect discrete morphologic defects, whereas compositional studies can identify biochemical changes in water permeability before other lesions develop (12).
- Although MRI is being used with more frequency to evaluate chondral injuries, arthroscopic evaluation remains the most accurate way to assess the location, depth, size, shape, and stability of a chondral or osteochondral defect of the articular surface. The Outerbridge classification is most widely used to grade these injuries (Table 7.1) (13). More recently, the International Cartilage Repair Society has modified this to a more comprehensive description and grading system (see Table 7.1) (14,15). The International Cartilage Repair Society grading system can be used to describe lesions both arthroscopically and using advanced radiologic imaging techniques.

NONSURGICAL TREATMENT

- Nonsurgical techniques are often used to manage patients' symptoms and slow the progression of the injury or disease. They may be considered based on patient age, activity level, and extent of the injury. As with most joint pathology, initial treatment of articular cartilage injuries is typically

Table 7.1 Outerbridge Arthroscopic Grading System and Modified International Cartilage Repair Society (ICRS) Classification System for Chondral Injury (13–15)

Grade of Injury	Outerbridge Arthroscopic Grading System	Modified ICRS System
Grade 0	Normal cartilage	Normal cartilage
Grade I	Cartilage with softening and swelling	Nearly normal with superficial fissuring
Grade II	Partial-thickness defect with fissures on the surface that do not reach subchondral bone or exceed 1.5 cm in diameter	Lesions extending less than 1/2 of cartilage depth
Grade III	Fissuring to the level of subchondral bone in an area with a diameter more than 1.5 cm	Lesions extending greater than 1/2 of cartilage depth up to subchondral plate
Grade IV	Exposed subchondral bone	Through subchondral plate, exposing subchondral bone

conservative with recommendations that include activity modification, physical therapy, judicious use of nonsteroidal anti-inflammatory drugs (NSAIDs), glucosamine and chondroitin sulfate, corticosteroid or biologic injections, and consideration for viscosupplementation (16).

- See Chapters 76–79 for further discussion of nonoperative therapies (Medications and Ergogenic Aids, Prolotherapy, Orthobiologic Therapies, and Joint Injections/Aspiration.)
- Patients with mechanical symptoms (including catching, locking, sensation of loose body, or giving way), acute motion loss, or failed nonsurgical management with pain and loss of function should be considered for surgical intervention.

SURGICAL TREATMENT

Arthroscopic Debridement and Lavage

- Arthroscopic debridement and lavage can be a first-line surgical intervention in a patient with a symptomatic articular cartilage injury. This treatment modality allows the surgeon to perform a diagnostic arthroscopy to assess for chondral injury and for concomitant pathologies in the remainder of the joint. Patient expectations must be managed in that the results of this procedure can range from diagnostic to therapeutic due to the removal of degenerative debris, loose nonviable chondral fragments, and lavage of the associated inflammatory cytokines such as interleukin-1 and tumor necrosis factor-α (17). Care is taken to preserve intact, healthy articular cartilage. Irrigation and debridement alone has been proven to provide good to excellent short- and medium-term benefits in 60%–70% of patients (17–19). In a select group of highly active individuals, especially in-season when return-to-sport times are critical, debridement may be a first-line option to provide beneficial, temporary improvement. In general, however, the results of arthroscopic debridement and lavage are often not durable and deteriorate over time, and the primary benefit that remains is the diagnostic information obtained to help guide future treatment decisions (Table 7.2) (24,27,29–32).

Fragment Fixation

- Osteochondral lesions occur most frequently on the femoral condylar surface, and can include a breath of pathology including osteochondritis dissecans, osteochondral defects, osteochondral fractures, and osteonecrosis (33). Fixation of these lesions is predicated on the condition, size, shape, defect location, and adequacy of subchondral bone attached to the osteochondral fragment. Radiographic and MRI evaluation can help with the determination of many of these factors and appropriateness of this surgical option. Prior to fixation of the osteochondral fragment, both the fragment and defect must be prepared to create an adequate healing milieu. The fragment must be reduced anatomically into its bed, and fixation may then be completed using either absorbable or nonabsorbable implants. Occasionally, bone graft augmentation is required for deeper cavitating lesions. Treating osteochondral lesions with the same considerations as a fracture nonunion will lead to more predictable healing. These factors include debriding fibrocartilage at the base of the lesion, microfracture augmentation of the base to promote bleeding, and rigid fixation with compression. Fixation is accomplished with the use of metal or composite bioabsorbable pins and screws. Metallic implants removed at 6–8 weeks allow the opportunity to verify fragment healing and prevent the untoward effects of prominent hardware that can develop over time (17). Successful healing of the osteochondral fragment with the use of headless metallic cannulated screws has been reported in up to 90% of patients and has demonstrated positive clinical and imaging outcomes at 10 years post operatively (34). Arthroscopic fixation of osteochondral lesions with bioabsorbable pins has also shown excellent clinical and radiographic results. Further use of bioabsorbable and next-generation fixation material will likely continue to become more prevalent. Benefits of bioabsorbable fixation include fewer procedures for implant removal, and lessened interference with imaging (35).

Marrow-Stimulating Techniques

- The goal of marrow stimulation techniques (MST) is to deliver mesenchymal stem cell progenitors to the bed of a focal chondral defect, which can lead to the subsequent formation of a fibrocartilage-like repair tissue from these cells.

Table 7.2 Results of Arthroscopic Debridement and Lavage

Study	No. of Patients	Mean Follow-Up	Results
Acosta et al., 2020 (20)	485	26.9 mo (8–40 mo)	Systematic review: Stable meniscal lesions <2 cm in size were effectively treated with debridement alone and showed significantly increased Lysholm and IKDC scores ($P < 0.005$).
Weißenberger et al., 2019 (21)	126	12 mo	Case-control study: Focal cartilage defects treated with debridement had overall improvement with respect to the KOOS. Lesser improvement in defects >2 cm^2.
Anderson et al., 2017 (22)	53	31.5 ± 13.9 mo	Retrospective case series: Improvement in all patient-reported outcome measures (PROM) except the mental component of the VR-12.
Kirkley et al., 2008 (23)	163	2 y	Randomized controlled trial: Arthroscopy and PT vs. PT alone showed no difference in WOMAC, or SF-36 between groups ($P = 0.22$).
Jackson and Dieterichs, 2003 (24)	121	4–6 y	Retrospective case series: Stage I: 100% excellent/good Stage II: 90.6% excellent/good Stage III: 48.7% excellent/good Stage IV: 11.9% excellent/good
Moseley et al., 2002 (25)	180	2 y	Randomized controlled trial: Debridement, lavage, and placebo showed no difference in KSPS, AIMS2-P, and SF-36 scores.
Steadman et al., 2001 (26)	75	11.3 y	Retrospective case series: Lysholm 58.8 → 89 Tegner 3.1 → 5.8 Work 4.9 → 7.6 Sports 4.2 → 7.1
Timoney et al., 1990 (27)	109	48 mo	Retrospective case series: 63% good 37% fair/poor
Jackson, 1989 (28)	137	3.5 y (2–9 y)	Retrospective case series: 68% remained improved
Sprague, 1981 (29)	78	14 mo	Retrospective case series: 74% good 26% fair/poor

AIMS2-P, Arthritis Impact Measurement Scales; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; KSPS, Knee-Specific Pain Scale; PT, physical therapy; SF-36, Short Form-36; VR-12, Veteran RAND 12-item health survey; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

This technique can be performed via drilling, abrasion, or microfracture and always involves penetration of the calcified cartilage layer into the subchondral bone to allow the migration of progenitor cells to the articular surface. In a 2021 retrospective comparative study of 68 patients, a battery-powered microdrilling technique demonstrated improved short-term outcomes compared to a traditional microfracture-and-awl technique (36). Microfracture can also be augmented with the local supplementation of chondrogenic growth factors to prolong the action of these mesenchymal stem cells (37). MST augmentation with a cartilage allograft extracellular matrix has recently been shown to improve outcomes with low complication rates at 2-year follow-up (38,39). Because of the limited fill that may occur in some lesions, particularly larger ones greater than 2 cm^2, and the different structural and biomechanical properties of this fibrocartilage-like repair tissue (see earlier Basic Science section), the best results are typically achieved with relatively small defects in a low-demand patient population (17). Results of microfracture technique are summarized in Table 7.3.

Osteochondral Autograft

- An osteochondral autograft transfer system (OATS) harvests plugs of native cartilage and bone from load-sparing areas of the knee and transfers them into the area of a symptomatic chondral defect. It offers several advantages, including increased generation of hyaline-like cartilage, a relatively brief rehabilitation period, and the ability to perform the procedure in a single operation (53). Return to sports has been found to be as low as 90 days in some studies (54). Limitations include the availability of low-contact harvest areas, donor site morbidity, and the potential for surface

Table 7.3 Results of Microfracture

Study	No.	Mean Follow-Up[a]	Results
Wen et al., 2022 (40)	Systematic review (635 patients)	2 y (1–5 y)	Systematic Review: Augmented microfracture with orthobiologics showed minimal improvement over traditional microfracture
Kim et al., 2020 (41)	Systematic review (29 studies)	≥2 y	Systematic Review: Autologous matrix-induced chondrogenesis vs microfracture showed no significant difference in clinical outcomes, other than IKDC subjective score
Orth et al., 2020 (42)	Systematic review (1759 patients)	6.6 y (4.3–8.8 y)	Systematic Review: Failure rates at 5 y: 11%–27% Failure rate at 10 y: 6%–32%
Mithoefer et al., 2012 (43)	21 professional athletes	13 y	Retrospective case series: Return to professional sport at 12 mo: 95% Years of subsequent professional play: 5 y (1–13 y)
Solheim et al., 2010 (44)	110 patients	5 y (2-9 y)	Retrospective cohort: Lysholm 51 → 71 VAS function 41 → 74 VAS pain 52 → 30[b]
Mithoefer et al., 2009 (45)	Systematic review (3122 patients)	3.4 ± 0.4 y (1–3 y)	Systematic review: Short-term clinical improvement rate (≤24 mo): 75%–100% Long-term clinical improvement rate (≥24 mo): 67%–80%
Asik et al., 2008 (46)	90 patients	5.2 y (2–9 y)	Retrospective case series: Lysholm 52.4 → 84.6 Tegner 2.6 → 5.2
Bae et al., 2006 (47)	47 knees	1 y	Second look arthroscopy: Extent of cartilage healing >90% in 55% of cases; 80%–89% in 10% Radiographic evaluation: average joint space increase of 1.06 mm on anterior-posterior and 1.37 mm on lateral
Gobbi et al., 2005 (48)	25 competitive athletes	6 y (3–10 y)	Prospective cohort study: 30% improved Lysholm 56.8 → 87.2 Tegner 3.2 → 5
Steadman et al., 2002 (49)	71 knees Age ≤ 45 y	11 y (7–17 y)	Retrospective case series: 80% improved Lysholm 59 → 89 Tegner 6 → 9 Majority of improvement in first year Maximal improvement in 2–3 y Younger patients did better
Steadman et al., 2001 (26)	75 patients	11.3 y	Retrospective case series: Lysholm 58.8 → 89 Tegner 3.1 → 5.8 Work 4.9 → 7.6 Sports 4.2 → 7.1
Gill and Macgillivray, 2001 (50)	103 patients	6 y (2–12 y)	Retrospective case series: 86% rated knee as normal/nearly normal Acute (treated within 12 wk) did better
Blevins et al., 1998 (51)	140 recreational athletes Mean age, 38 y Mean defect size, 2.8 cm^2 38 high-level athletes Mean age, 26 y Mean defect size, 2.2 cm^2	3.7 y	Prospective cohort study: 77% returned to sports
Steadman et al., 1997 (52)	203 patients	3 y (2–12 y)	Retrospective case series: 75% improved, 19% unchanged, 6% worse, 60% improved sports Poor prognosis: joint space narrowing, age >30 y, no postoperative CPM

CPM, continuous passive motion; IKDC, International Knee Documentation Committee; VAS, visual analog scale.
[a]Represents median number of years as reported by study.
[b]Lower values denote improvement.

plug incongruity, although advances in computer modeling have improved donor site matching (55–57). Patient selection is critical and, in general, is recommended for lesions <2–3 cm^2 (58). Short- and mid-term results of this technique have been promising, showing greater than 90% good to excellent results and a 78% survival rate at 10 years (59–61).

Osteochondral Allograft

- Osteochondral allograft transplantation is a commonly used procedure used to treat lesions of the knee, shoulder, ankle, and hip. It involves transplantation of a prolonged, freshly preserved (at 4 or 37°C) cadaveric graft consisting of intact, viable hyaline cartilage, and its underlying subchondral bone into the articular cartilage defect. Because other preservation techniques such as fresh-freezing, freeze-drying, and cryopreservation have been shown to decrease chondrocyte viability and ultimate load and increase stiffness, fresh osteochondral allografts are typically used (62,63). This procedure is ideal for lesions that are large, multifocal, multicompartmental, or present with significant subchondral bone loss. It allows for a shorter operative time, replication of native knee anatomy, immediate transplantation of both cartilage and subchondral bone as a single-stage procedure, a lower incidence of postoperative arthrofibrosis, and no donor site morbidity (64).
- Limitations include concerns over insurance approval, graft availability, low but possible risk of immunologic rejection, potential for disease transmission, adequate graft healing and technically demanding aspects of graft matching and sizing (62,64,65). Incorporation of graft preparation techniques prior to implantation have shown to have utmost importance in minimizing some of these concerns. Some recent advances include pulsed lavage, pressurized CO_2, biologic augmentation, and minimizing impaction loads during graft insertion (66–69).
- Use of osteochondral allografts (OAGs) in recent years have increased due to the ability to reliably improve patient-reported outcomes (PROs) and longevity after graft incorporation into host tissue (70). There are a number of well-demonstrated long-term clinical follow-up studies that demonstrate an average of 88% success at 5 years and 81% success at 10 years after surgery (59,64,71–74). In addition, a recent comprehensive review evaluating 205 patients demonstrated improvement in Lysholm scores (20,61–87), International Knee Documentation Committee (IKDC) scores (54–84), all five components of the Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain, 57–76; Other Disease-Specific Symptoms, 55–73; Activities of Daily Living Function, 65–86; Sport and Recreation Function, 26–56; Knee-Related Quality of Life, 23–56), and Short Form-12 physical component scores (55–66,71). Literature outcomes on osteochondral allografts are included in Table 7.4.
- Although osteochondral allograft transplantation was popularized initially for focal articular cartilage injuries of the femoral condyles, the technique has proven efficacious for patellofemoral chondral injuries. In a systematic review of 129 patients across eight studies, OAGs conferred significant improvements in multiple patient-reported outcomes with a mean 77.2% survival at 10 years. OAG for patellofemoral defects was also associated with a higher rate of concomitant procedures, and therefore the relative contributions of individual procedures require further study (75).

Autologous Chondrocyte Implantation

- Autologous chondrocyte implantation requires a two-stage procedure including the biopsy of chondrocytes from the knee, culturing and expansion of the chondrocyte cell line, and reoperation for transplantation into the cartilage defect beneath a periosteal or collagen matrix patch. The potential advantages of this procedure include the ability to fill defects as large as 10 cm^2, the development of hyaline-like cartilage rather than fibrocartilage in the grafted defect, and possibly better long-term outcomes and longevity of the healing tissue. This procedure can be technically demanding, requiring the patient to undergo a relatively long rehabilitation in addition to a requirement for two surgical procedures. In addition, although the overall complication rate appears to be relatively low, the adverse events that do occur following autologous chondrocyte implantation can result in subsequent operative intervention.
- Peterson et al. demonstrated that 92% of patients were satisfied and would have the autologous chondrocyte implantation (ACI) surgery again at 10–20 years after transplantation. In their cohort of 50 patients, Micheli et al. demonstrated that 84% of patients had significant improvement in their symptoms at 3 years postoperatively. A recent multicenter cohort study evaluated outcomes of autologous chondrocyte transplantation after failed previous articular cartilage surgery (76). After 48 months of follow-up, 76% of the 154 patients had a successful outcome, whereas 24% were deemed as having treatment failure. Interestingly, 49% of the patients (n = 76) had a subsequent surgical procedure performed after the autologous chondrocyte implantation. These additional procedures, predominantly arthroscopic, were not predictive of failure. The use of type I/III bilayer collagen instead of a periosteal patch to cover the cells during the implantation procedure has been shown to decrease the reoperation rate significantly (77). A recent study evaluating 2- to 9-year outcomes of autologous chondrocyte implantation in a diverse patient population demonstrated that 75% of patients were completely or mostly satisfied with their outcomes and 83% would have the procedure done again (78,79).
- In 2016, matrix-induced autologous chondrocyte implantation (MACI; autologous cultured chondrocytes on porcine collagen membrane) received approval from the U.S. Food and Drug Administration for the treatment of symptomatic articular cartilage defects of the knee in adults with

Table 7.4 Results of Osteochondral Allograft

Study	No.	Location	Mean Follow-Up	Results
Gilat et al., 2021 (71)	205	F	7.7 y	Case series: 86% success rate at 5 y 82% success rate at 10 y 21% failure
Familiari et al., 2018 (59)	1036	F, T, P	8.7 y	Systematic review: 87% success rate at 5 y 79% success rate at 10 y 73% success rate at 15 y 68% success rate at 20 y 18% failure
Frank et al., 2017 (64)	224	F	5 y	Case series: 87% success rate at 5 y 18% failure
Assenmacher et al., 2016 (65)	291	F, T, P	12.3 y	Systematic review: 75% success rate 25% failure
Cameron et al., 2016 (72)	28	F	7 y	Case series: 100% success rate at 5 y 92% success rate at 10 y 85% good/excellent
Briggs et al., 2015 (73)	55	F, T, P	>7.6 y	Case series: 90% success rate at 5 y 75% success rate at 10 y 85% good/excellent 6% fair/poor
Gracitelli et al., 2015 (74)	28	P	9.7 y	Case series: 78% success rate at 5 y 78% success rate at 10 y 56% success rate at 15 y 29% failure

F, femur; IKDC, International Knee Documentation Committee; P, patella; T, tibia.

or without bone involvement (80). This approval was supported by the results of the European SUMMIT (Superiority of MACI Implant vs. Microfracture Treatment) trial, which found clinically and statistically significant improvements in MACI over microfracture treatment with regard to KOOS pain and function sub-scores (81). In addition, Ebert et al. demonstrated significant improvements in MRI-based scores after 10 years postoperatively, as well as high patient satisfaction rates with the outcome of their surgery, improvement in knee pain relief, and ability to participate in sport again. Outcomes of autologous chondrocyte implantation from various studies over the years are summarized in Table 7.5.

TREATMENT DECISION MAKING

- Management of articular cartilage injuries can be challenging, and there are multiple options available to treat similar lesions. Although there is no consensus on optimal treatment, certain guidelines can be followed. Decision making must consider patient goals, physical demands, expectations, and perceptions, as well as objective measurements such as defect size, depth, location, chronicity, previous treatments and responses, and concomitant pathology. Ligament insufficiency, meniscal pathology, and/or mechanical malalignment must be addressed, particularly in the treatment of articular cartilage injury of the femoral condyles. It is common for concomitant procedures to be performed, including meniscal allograft transplantation, distal femoral or high tibial osteotomy, and tibial tuberosity elevation. Our recommended primary treatment guideline is included in Figure 7.1.
- Articular cartilage surgical restoration allows for a high rate of return to high-impact sports, often at the preinjury competitive level. The time of return and durability can be variable and depend on repair technique and athlete-specific factors. Player age, competitive level, defect size, time to treatment, and repair tissue morphology all affect the ability and time to return-to-play. Sports participation after cartilage repair generally promotes joint restoration and functional recovery. Time to return to impact sports generally varies between 7 and 17 months, with the longest time after autologous chondrocyte transplantation.

Table 7.5 Results of Autologous Chondrocyte Transplantation

Study	No.	Location	Mean Follow-Up	Results
Ebert et al., 2020 (88)	70	F	>10 y, Range 10.5–11.5 y	Prospective randomized trial: Significant improvement in all clinical measures employed and MRI-based scores ($P < 0.05$) 88.3% patient satisfaction with the 10-y results of their surgery 93.3% patient satisfaction with the improvement in knee pain relief 88.3% patient satisfaction with the improvement in their ability to participate in sport
Saris et al., 2014 (81)	144	F	2 y	Prospective randomized trial: Statistically significant improvements in KOOS pain (11.76, $P < 0.001$) and function subscores (11.41, $P = 0.016$) over microfracture treatment Significant improvement for MACI over microfracture treatment observed in as early as 36 wk and maintained throughout study
Moseley et al., 2010 (89)	72	F	>5 y Mean, 9.2 y	Case series: 69% of patients improved from baseline 12.5% had no change 17% failed
Peterson et al., 2010 (90)	224	F, P, multiple	>10 y Mean, 12.8 y	Case series: 92% patient satisfaction
Bhosale et al., 2009 (91)	80	F, P, Tr, multiple	>2.7 y Mean, 5 y	Prospective cohort study: 81% clinical improvement 19% clinical decline
Peterson et al., 2002 (92)	18 14 17 11	F OCD P F/ACL	>5 y >5 y >5 y >5 y	Case series: 89% good/excellent 86% good/excellent 65% good/excellent 91% good/excellent
Micheli et al., 2001 (93)	50	F/Tr/P	>3 y	Prospective cohort study: 84% significant improvement 2% unchanged 13% declined
Peterson et al., 2000 (79)	25 19 16 16	F P F/ACL Multiple	>2 y >2 y >2 y >2 y	Case series: 92% good/excellent 62% good/excellent 75% good/excellent 67% good/excellent
Gillogly et al., 1998 (94)	25	F, P, T	>1 y	Case series: 88% good/excellent
Brittberg et al., 1994 (95)	16 7	F P	39 mo 36 mo	Prospective cohort study: 88% good/excellent 12% poor 29% good/excellent 71% fair/poor

ACL, anterior cruciate ligament; F, femur; KOOS, Knee Injury and Osteoarthritis Score; MACI, autologous cultured chondrocytes on porcine collagen membrane; MRI, magnetic resonance imaging; OCD, osteochondritis dissecans; P, patella; T, tibia; Tr, trochlea.

FUTURE DIRECTIONS

- Ongoing research in the area of articular cartilage continues. Indeed, it is one of the most studied topics in contemporary orthopedics. Additional treatments being evaluated include the incorporation of orthobiologic agents, including bone marrow aspirate concentrate (BMAC), platelet-rich plasma (PRP), cell-based therapies, amniotic suspension allografts, and adipose tissue with the above procedures.

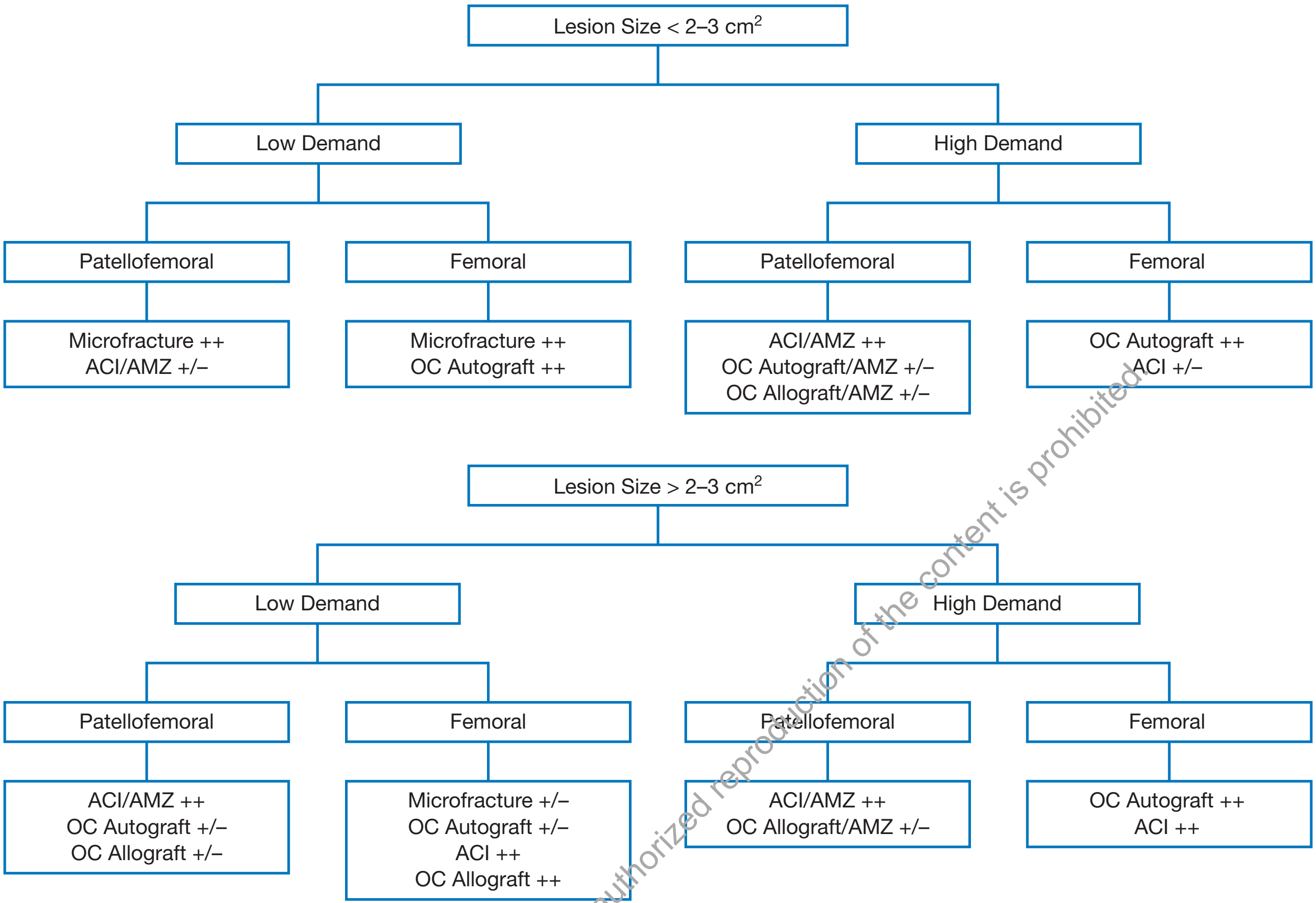

Figure 7.1: Surgical treatment algorithm of articular cartilage injuries. ACI, autologous chondrocyte implantation; AMZ, anteromedialization tibial tubercle osteotomy; OC, osteochondral.

These techniques involve delivery of growth factors, naturally derived blood components, and autologous tissue to the surgical site that have the potential to enhance healing and repair of the cartilage following the procedure. Human, animal, and basic science models have demonstrated early promise using these techniques; however, more rigorous, well-conducted human trials need be conducted to elucidate the scope of additional benefits associated with them (82–87).

REFERENCES

1. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. *Arthroscopy*. 1997 Aug;13(4):456–60.
2. Cole B, Frederick R, Levy A, Zaslav K. Management of a 37-year-old man with recurrent. *Knee Pain*. 1999;6(6).
3. Frank RM, Cotter EJ, Hannon CP, Harrast JJ, Cole BJ. Cartilage restoration surgery: incidence rates, complications, and trends as reported by the American board of orthopaedic surgery Part II candidates. *Arthroscopy*. 2019 Jan;35(1):171–8.
4. Gowd AK, Cvetanovich GL, Liu JN, et al. Management of chondral lesions of the knee: analysis of trends and short-term complications using the national surgical quality improvement program database. *Arthroscopy*. 2019 Jan;35(1):138–46.
5. Buckwalter J, Rosenberg L, Hunziker E. Articular cartilage: composition and structure. In: *Injury and Repair of the Musculoskeletal Soft Tissues*; 1988:405–25.
6. Sophia Fox AJ, Bedi A, Rodeo SA. The basic science of articular cartilage: structure, composition, and function. *Sports Health*. 2009 Nov;1(6):461–8.
7. Buckwalter JA. Articular cartilage injuries. *Clin Orthop Relat Res*. 2002 Sep;402:21–37.
8. Krych AJ, Saris DBF, Stuart MJ, Hacken B. Cartilage injury in the knee: assessment and treatment options. *J Am Acad Orthop Surg*. 2020 Nov;28(22):914–22.
9. Gilat R, Haunschild ED, Patel S, et al. Understanding the difference between symptoms of focal cartilage defects and osteoarthritis of the knee: a matched cohort analysis. *Int Orthop*. 2021 Jul;45(7):1761–6.
10. Khanna AJ, Cosgarea AJ, Mont MA, et al. Magnetic resonance imaging of the knee. Current techniques and spectrum of disease. *J Bone Joint Surg Am*. 2001;83-A(suppl 2 pt 2):128–41.
11. Bauer JS, Barr C, Henning TD, et al. Magnetic resonance imaging of the ankle at 3.0 Tesla and 1.5 Tesla in human cadaver specimens with artificially created lesions of cartilage and ligaments. *Investig Radiol*. 2008 Sep;43(9):604–11.

12. Strickland CD, Ho CK, Merkle AN, Vidal AF. MR imaging of knee cartilage injury and repair surgeries. *Magn Reson Imaging Clin N Am*. 2022 May;30(2):227–39.
13. Outerbridge RE. The etiology of chondromalacia patellae. 1961. *Clin Orthop Relat Res*. 2001 Aug;389:5–8.
14. Brittberg M, Winalski CS. Evaluation of cartilage injuries and repair. *J Bone Joint Surg Am*. 2003;85-A(suppl 2):58–69.
15. Mainil-Varlet P, Aigner T, Brittberg M. International Cartilage Repair Society, et al. Histological assessment of cartilage repair: a report by the histology Endpoint Committee of the International cartilage repair Society (ICRS). *J Bone Joint Surg Am*. 2003;85-A(suppl 2):45–57.
16. Daher RJ, Chahine NO, Greenberg AS, Sgaglione NA, Grande DA. New methods to diagnose and treat cartilage degeneration. *Nat Rev Rheumatol*. 2009 Nov;5(11):599–607.
17. Alford JW, Cole BJ. Cartilage restoration, Part 2: techniques, outcomes, and future directions. *Am J Sports Med*. 2005 Mar;33(3):443–60.
18. Friedman MJ, Berasi CC, Fox JM, Del Pizzo W, Snyder SJ, Ferkel RD. Preliminary results with abrasion arthroplasty in the osteoarthritic knee. *Clin Orthop Relat Res*. 1984;182:200–5.
19. Totlis T, Marín Fermín T, Kalifis G, Terzidis I, Maffulli N, Papakostas E. Arthroscopic debridement for focal articular cartilage lesions of the knee: a systematic review. *Surgeon*. 2021 Dec;19(6):356–64.
20. Acosta J, Ravaei S, Brown SM, Mulcahey MK. Examining techniques for treatment of medial meniscal Ramp lesions during anterior cruciate ligament reconstruction: a systematic review. *Arthroscopy*. 2020 Nov;36(11):2921–33.
21. Weißenberger M, Heinz T, Boelch SP, et al. Is debridement beneficial for focal cartilage defects of the knee: data from the German Cartilage Registry (KnorpelRegister DGOU). *Arch Orthop Trauma Surg*. 2020 Mar;140(3):373–82.
22. Anderson DE, Rose MB, Wille AJ, Wiedrick J, Crawford DC. Arthroscopic mechanical chondroplasty of the knee is beneficial for treatment of focal cartilage lesions in the absence of concurrent pathology. *Orthop J Sports Med*. 2017 May;5(5):2325967117707213.
23. Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med*. 2008 Sep;359(11):1097–107.
24. Jackson RW, Dieterichs C. The results of arthroscopic lavage and debridement of osteoarthritic knees based on the severity of degeneration: a 4- to 6-year symptomatic follow-up. *Arthroscopy*. 2003 Jan;19(1):13–20.
25. Moseley JB, O'Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med*. 2002 Jul;347(2):81–8.
26. Steadman JR, Rodkey WG, Rodrigo JJ. Microfracture: surgical technique and rehabilitation to treat chondral defects. *Clin Orthop Relat Res*. 2001 Oct;391(suppl l):S362–9.
27. Timoney JM, Kneisl JS, Barrack RL, Alexander AH. Arthroscopy update #6. Arthroscopy in the osteoarthritic knee. Long-term follow-up. *Orthop Rev*. 1990 Apr;19(4):371–9.
28. Jackson RW. Meniscal and articular cartilage injury in sport. *J R Coll Surg Edinb*. 1989;34(6 suppl l):S15–7.
29. Sprague NF. Arthroscopic debridement for degenerative knee joint disease. *Clin Orthop Relat Res*. 1981 Oct;160:118–23.
30. Bernard J, Lemon M, Patterson MH. Arthroscopic washout of the knee-a 5-year survival analysis. *Knee*. 2004 Jun;11(3):233–5.
31. Hubbard MJ. Arthroscopic surgery for chondral flaps in the knee. *J Bone Joint Surg Br*. 1987 Nov;69(5):794–6.
32. Oliver-Welsh L, Griffin JW, Meyer MA, Gitelis ME, Cole BJ. Deciding how best to treat cartilage defects. *Orthopedics*. 2016 Nov;39(6):343–50.
33. Cordunianu MA, Antoniac I, Niculescu M, et al. Treatment of knee osteochondral fractures. *Healthcare (Basel)*. 2022 Jun;10(6):1061.
34. Ackermann J, Waltenspül M, Merkely G, et al. Association of subchondral changes with age and clinical outcome in patients with osteochondral fractures in the knee: MRI analysis at 1 to 10 Years postoperatively. *Orthop J Sports Med*. 2022 Jul;10(7):23259671221113234.
35. Komnos G, Iosifidis M, Papageorgiou F, Melas I, Metaxiotis D, Hantes M. Juvenile osteochondritis dissecans of the knee joint: midterm clinical and MRI outcomes of arthroscopic retrograde drilling and internal fixation with bioabsorbable pins. *Cartilage*. 2021 Dec;13(1 suppl):1228S–36S.
36. Beletsky A, Naveen NB, Tauro T, et al. Microdrilling demonstrates superior patient-reported outcomes and lower revision rates than traditional microfracture: a matched cohort analysis. *Arthrosc Sports Med Rehabil*. 2021 Jun;3(3):e629–38.
37. Strauss EJ, Barker JU, Kercher JS, Cole BJ, Mithoefer K. Augmentation strategies following the microfracture technique for repair of focal chondral defects. *Cartilage*. 2010 Apr;1(2):145–52.
38. Cole BJ, Haunschild ED, Carter T, Meyer J, Fortier LA, Gilat R, BC BioCartilage Study Group. Clinically significant outcomes following the treatment of focal cartilage defects of the knee with microfracture augmentation using cartilage allograft extracellular matrix: a multicenter prospective study. *Arthroscopy*. 2021 May;37(5):1512–21.
39. Brusalis CM, Greditzer HG, Fabricant PD, Stannard JP, Cook JL. BioCartilage augmentation of marrow stimulation procedures for cartilage defects of the knee: two-year clinical outcomes. *Knee*. 2020 Oct;27(5):1418–25.
40. Wen HJ, Yuan LB, Tan HB, Xu YQ. Microfracture versus enhanced microfracture techniques in knee cartilage restoration: a systematic review and meta-analysis. *J Knee Surg*. 2022 Jun;35(7):707–17.
41. Kim JH, Heo JW, Lee DH. Clinical and radiological outcomes after autologous matrix-induced chondrogenesis versus microfracture of the knee: a systematic review and meta-analysis with a minimum 2-year follow-up. *Orthop J Sports Med*. 2020 Nov;8(11):2325967120959280.
42. Orth P, Gao L, Madry H. Microfracture for cartilage repair in the knee: a systematic review of the contemporary literature. *Knee Surg Sports Traumatol Arthrosc*. 2020 Mar;28(3):670–706.
43. Mithoefer K, Steadman RJ. Microfracture in football (Soccer) Players: a case Series of Professional athletes and systematic review. *Cartilage*. 2012 Jan;3(1 suppl l):18S–24S.
44. Solheim E, Øyen J, Hegna J, Austgulen OK, Harlem T, Strand T. Microfracture treatment of single or multiple articular cartilage defects of the knee: a 5-year median follow-up of 110 patients. *Knee Surg Sports Traumatol Arthrosc*. 2010 Apr;18(4):504–8.
45. Mithoefer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. *Am J Sports Med*. 2009 Oct;37(10):2053–63.
46. Asik M, Ciftci F, Sen C, Erdil M, Atalar A. The microfracture technique for the treatment of full-thickness articular cartilage lesions of the knee: midterm results. *Arthroscopy*. 2008 Nov;24(11):1214–20.
47. Bae DK, Yoon KH, Song SJ. Cartilage healing after microfracture in osteoarthritic knees. *Arthroscopy*. 2006 Apr;22(4):367–74.
48. Gobbi A, Nunag P, Malinowski K. Treatment of full thickness chondral lesions of the knee with microfracture in a group of athletes. *Knee Surg Sports Traumatol Arthrosc*. 2005 Apr;13(3):213–21.
49. Steadman JR, Rodkey WG, Briggs KK. Microfracture to treat full-thickness chondral defects: surgical technique, rehabilitation, and outcomes. *J Knee Surg*. 2002;15(3):170–6.
50. Gill TJ, Macgillivray JD. The technique of microfracture for the treatment of articular cartilage defects in the knee. *Operat Tech Orthop*. 2001 Apr;11(2):105–7.

51. Blevins FT, Steadman JR, Rodrigo JJ, Silliman J. Treatment of articular cartilage defects in athletes: an analysis of functional outcome and lesion appearance. *Orthopedics*. 1998 Jul;21(7):761–8.
52. Steadman JR, Rodkey WG, Singleton SB, Briggs KK. Microfracture technique for full-thickness chondral defects: technique and clinical results. *Operat Tech Orthop*. 1997;7(4):300–4.
53. Riboh JC, Cvetanovich GL, Cole BJ, Yanke AB. Comparative efficacy of cartilage repair procedures in the knee: a network meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. 2017 Dec;25(12):3786–99.
54. Werner BC, Cosgrove CT, Gilmore CJ, et al. Accelerated return to sport after osteochondral autograft plug transfer. *Orthop J Sports Med*. 2017 Apr;5(4):2325967117702418.
55. Bartz RL, Kamaric E, Noble PC, Lintner D, Bocell J. Topographic matching of selected donor and recipient sites for osteochondral autografting of the articular surface of the femoral condyles. *Am J Sports Med*. 2001;29(2):207–212.
56. Feczkó P, Hangody L, Varga J, et al. Experimental results of donor site filling for autologous osteochondral mosaicplasty. *Arthroscopy*. 2003 Sep;19(7):755–61.
57. LaPrade RF, Botker JC. Donor-site morbidity after osteochondral autograft transfer procedures. *Arthroscopy*. 2004 Sep;20(7):e69–73.
58. Dekker TJ, Aman ZS, DePhillipo NN, Dickens JF, Anz AW, LaPrade RF. Chondral lesions of the knee: an evidence-based approach. *J Bone Joint Surg Am*. 2021 Apr 7;103(7):629–45.
59. Familiari F, Cinque ME, Chahla J, et al. Clinical outcomes and failure rates of osteochondral allograft transplantation in the knee: a systematic review. *Am J Sports Med*. 2018 Dec;46(14):3541–9.
60. Hangody L, Feczkó P, Bartha L, Bodó G, Kish G. Mosaicplasty for the treatment of articular defects of the knee and ankle. *Clin Orthop Relat Res*. 2001 Oct;391(suppl l):S328–36.
61. Hangody L, Kish G, Kárpáti Z, Udvarhelyi I, Szigeti I, Bély M. Mosaicplasty for the treatment of articular cartilage defects: application in clinical practice. *Orthopedics*. 1998 Jul;21(7):751–6.
62. Beer AJ, Tauro TM, Redondo ML, Christian DR, Cole BJ, Frank RM. Use of allografts in orthopaedic surgery: safety, procurement, storage, and outcomes. *Orthop J Sports Med*. 2019 Dec;7(12):2325967119891435.
63. Wagner KR, DeFroda SF, Sivasundaram L, et al. Osteochondral allograft transplantation for focal cartilage defects of the femoral condyles. *JBJS Essent Surg Tech*. 2022;12(3):e21.00037.
64. Frank RM, Lee S, Levy D, et al. Osteochondral allograft transplantation of the knee: analysis of failures at 5 years. *Am J Sports Med*. 2017 Mar;45(4):864–74.
65. Assenmacher AT, Pareek A, Reardon PJ, Macalena JA, Stuart MJ, Krych AJ. Long-term outcomes after osteochondral allograft: a systematic review at long-term follow-up of 12.3 years. *Arthroscopy*. 2016 Oct;32(10):2160–8.
66. Sun Y, Jiang W, Cory E, et al. Pulsed lavage cleansing of osteochondral grafts depends on lavage duration, flow intensity, and graft storage condition. *PLoS One*. 2017;12(5):e0176934.
67. Yanke A, Dandu N, Bodendorfer B, et al. Paper 18: effect of bone marrow aspirate concentrate on osteochondral allograft transplantation incorporation – a prospective, randomized, single blind investigation. *Orthop J Sports Med*. 2022 Jul;10(7 suppl 5):2325967121S00582.
68. Meyer MA, McCarthy MA, Gitelis ME, et al. Effectiveness of lavage techniques in removing immunogenic elements from osteochondral allografts. *Cartilage*. 2017 Oct;8(4):369–73.
69. Kang RW, Friel NA, Williams JM, Cole BJ, Wimmer MA. Effect of impaction sequence on osteochondral graft damage: the role of repeated and varying loads. *Am J Sports Med*. 2010 Jan;38(1):105–13.
70. Wagner KR, Kaiser JT, DeFroda SF, Meeker ZD, Cole BJ. Rehabilitation, restrictions, and return to sport after cartilage procedures. *Arthrosc Sports Med Rehabil*. 2022 Jan;4(1):e115–24.
71. Gilat R, Haunschild ED, Huddleston HP, et al. Osteochondral allograft transplant for focal cartilage defects of the femoral condyles: clinically significant outcomes, failures, and survival at a minimum 5-year follow-up. *Am J Sports Med*. 2021 Feb;49(2):467–75.
72. Cameron JI, Pulido PA, McCauley JC, Bugbee WD. Osteochondral allograft transplantation of the femoral trochlea. *Am J Sports Med*. 2016 Mar;44(3):633–8.
73. Briggs DT, Sadr KN, Pulido PA, Bugbee WD. The use of osteochondral allograft transplantation for primary treatment of cartilage lesions in the knee. *Cartilage*. 2015 Oct;6(4):203–7.
74. Gracitelli GC, Meric G, Pulido PA, Görtz S, De Young AJ, Bugbee WD. Fresh osteochondral allograft transplantation for isolated patellar cartilage injury. *Am J Sports Med*. 2015 Apr;43(4):879–84.
75. Chahla J, Sweet MC, Okoroha KR, et al. Osteochondral allograft transplantation in the patellofemoral joint: a systematic review. *Am J Sports Med*. 2019 Oct;47(12):3009–18.
76. Zaslav K, Cole B, Brewster R, STAR Study Principal Investigators, et al. A prospective study of autologous chondrocyte implantation in patients with failed prior treatment for articular cartilage defect of the knee: results of the Study of the Treatment of Articular Repair (STAR) clinical trial. *Am J Sports Med*. 2009 Jan;37(1):42–55.
77. Gomoll AH, Probst C, Farr J, Cole BJ, Minas T. Use of a type I/III bilayer collagen membrane decreases reoperation rates for symptomatic hypertrophy after autologous chondrocyte implantation. *Am J Sports Med*. 2009 Nov;37(suppl 1):20S–3S.
78. McNickle AG, L'Heureux DR, Yanke AB, Cole BJ. Outcomes of autologous chondrocyte implantation in a diverse patient population. *Am J Sports Med*. 2009 Jul;37(7):1344–50.
79. Peterson L, Minas T, Brittberg M, Nilsson A, Sjögren-Jansson E, Lindahl A. Two- to 9-year outcome after autologous chondrocyte transplantation of the knee. *Clin Orthop Relat Res*. 2000 May;374:212–34.
80. Carey JL, Remmers AE, Flanigan DC. Use of MACI (autologous cultured chondrocytes on porcine collagen membrane) in the United States: preliminary experience. *Orthop J Sports Med*. 2020 Aug;8(8):2325967120941816.
81. Saris D, Price A, Widuchowski W, SUMMIT study group, et al. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: two-year follow-up of a prospective randomized trial. *Am J Sports Med*. 2014 Jun;42(6):1384–94.
82. Oladeji LO, Stannard JP, Cook CR, et al. Effects of autogenous bone marrow aspirate concentrate on radiographic integration of femoral condylar osteochondral allografts. *Am J Sports Med*. 2017 Oct;45(12):2797–803.
83. Enea D, Cecconi S, Calcagno S, Busilacchi A, Manzotti S, Gigante A. One-step cartilage repair in the knee: collagen-covered microfracture and autologous bone marrow concentrate. A pilot study. *Knee*. 2015 Jan;22(1):30–35.
84. Gigante A, Cecconi S, Calcagno S, Busilacchi A, Enea D. Arthroscopic knee cartilage repair with covered microfracture and bone marrow concentrate. *Arthrosc Tech*. 2012 Dec;1(2):e175–80.
85. Ow ZGW, Cheang HLX, Koh JH, et al. Does the choice of acellular scaffold and augmentation with bone marrow aspirate concentrate affect short-term outcomes in cartilage repair? A systematic review and meta-analysis. *Am J Sports Med*. 2023 May;51(6):1622–33.
86. Dávila Castrodad IM, Kraeutler MJ, Fasulo SM, Festa A, McInerney VK, Scillia AJ. Improved outcomes with arthroscopic bone marrow aspirate concentrate and cartilage-derived matrix implantation versus chondroplasty for the treatment of focal chondral defects of the knee joint: a retrospective case series. *Arthrosc Sports Med Rehabil*. 2022 Apr;4(2):e411–6.

87. Meng HYH, Lu V, Khan W. Adipose tissue-derived mesenchymal stem cells as a potential restorative treatment for cartilage defects: a PRISMA review and meta-analysis. *Pharmaceuticals*. 2021 Dec 8;14(12):1280.
88. Ebert JR, Fallon M, Ackland TR, Janes GC, Wood DJ. Minimum 10-year clinical and radiological outcomes of a randomized controlled trial evaluating 2 different approaches to full weightbearing after matrix-induced autologous chondrocyte implantation. *Am J Sports Med*. 2020 Jan;48(1):133–42.
89. Moseley JB, Anderson AF, Browne JE, et al. Long-term durability of autologous chondrocyte implantation: a multicenter, observational study in US patients. *Am J Sports Med*. 2010 Feb;38(2):238–46.
90. Peterson L, Vasiliadis HS, Brittberg M, Lindahl A. Autologous chondrocyte implantation: a long-term follow-up. *Am J Sports Med*. 2010 Jun;38(6):1117–24.
91. Bhosale AM, Kuiper JH, Johnson WEB, Harrison PE, Richardson JB. Midterm to long-term longitudinal outcome of autologous chondrocyte implantation in the knee joint: a multilevel analysis. *Am J Sports Med*. 2009 Nov;37(suppl 1):131S–8S.
92. Peterson L, Brittberg M, Kiviranta I, Akerlund EL, Lindahl A. Autologous chondrocyte transplantation. Biomechanics and long-term durability. *Am J Sports Med*. 2002;30(1):2–12.
93. Micheli LJ, Browne JE, Erggelet C, et al. Autologous chondrocyte implantation of the knee: multicenter experience and minimum 3-year follow-up. *Clin J Sport Med*. 2001 Oct;11(4):223–8.
94. Gillogly SD, Voight M, Blackburn T. Treatment of articular cartilage defects of the knee with autologous chondrocyte implantation. *J Orthop Sports Phys Ther*. 1998 Oct;28(4):241–51.
95. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med*. 1994 Oct 6;331(14):889–95.