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Management of Articular Cartilage Defects in the Knee: An Evidence-Based Algorithm

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Abstract

Focal articular cartilage lesions of the knee are a challenging disease entity due to the poor regenerative properties of hyaline cartilage that often lead to degenerative joint disease. Surgery is indicated to alleviate symptoms, restore function, and return to desired activities when conservative treatment fails. Providers must consider defect size and severity, compliance with the postoperative rehabilitation protocol including weight-bearing restrictions, and patient expectations in their clinical decision-making. Smaller defects may be treated with arthroscopic chondroplasty, bone marrow stimulation, and osteochondral autologous transfer. Alternative surgical options for larger defects include osteochondral restoration using fresh vs. cryopreserved allografts, autologous chondrocyte implantation, and particulated juvenile allograft cartilage. This article will review available treatment options and provide an evidence-based treatment algorithm to guide the orthopaedic clinician's clinical decision-making.

Introduction

Chondral defects of the knee affect over 900,000 people in the United States, resulting in over 200,000 surgical treatments annually[1]. Articular cartilage lesions are seen in over 60% of patients undergoing knee arthroscopy and are most commonly found on the lateral aspect of the medial femoral condyle[1,2]. Over 50% of these patients have large focal lesions ($\geq$2 cm^2) and are twice as likely to undergo knee arthroplasty compared with patients with small defects ($<$2 cm^2)[2,3].

Hyaline articular cartilage is a highly specialized connective tissue composed of a dense extracellular matrix (ECM) of water, collagen type II, proteoglycans, and a low cell density of chondrocytes[4]. The limited proliferation rate of these chondrocytes, combined with the poor vascularity of hyaline cartilage, limits the regenerative capacity of hyaline cartilage. Contact stresses are shifted to the surrounding healthy cartilage when a chondral defect is present, which can lead to degenerative knee osteoarthritis (OA)[5-7].

Nonoperative treatment is often the first-line management for focal cartilage lesions; however, up to 90% of patients treated with conservative management experience continued pain and mechanical symptoms requiring operative intervention[7,8]. Surgical treatment options are dependent on defect size and severity, compliance with the postoperative rehabilitation protocol including weight-bearing restrictions, and patient goals and expectations[9,10]. With such complex decision-making, it is important for clinicians to understand appropriate diagnostic measures, treatment options, and patient selection criteria when determining the optimal treatment. This article will review surgical interventions for knee focal articular cartilage lesions and provide an evidence-based treatment algorithm to guide clinical decision-making to optimize pain, function, and return to sport.

History and Physical Examination

A thorough patient history and physical examination including mechanism of

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injury, physical activity, work requirements, and previous surgical and nonoperative interventions are essential. Patients presenting with articular cartilage defects often complain of knee pain with activity, intermittent stiffness and swelling, and functional limitations.

Before surgical intervention is considered, concomitant ligamentous, meniscal, and alignment pathology must be evaluated to optimize success. The presence of any associated anterior cruciate ligament injury (positive Lachman), posterior cruciate ligament injury (positive posterior drawer), or meniscal pathology (joint line tenderness, positive McMurray test, and positive Apley test) should also be evaluated.

The 2000 International Knee Documentation Committee (IKDC) Knee Examination Form can be used as a comprehensive guide for standardized knee evaluation, containing both objective and patient-reported subjective sections[11]. The IKDC evaluates 7 variables including effusion, passive range of motion (ROM), ligamentous laxity, compartmental crepitus, harvest site pathology, x-ray findings, and functional tests[11]. Effusion is evaluated using the Ballottement test and graded as none, mild, moderate, or severe. Knee flexion and extension ROM are measured using a goniometer and compared with the contralateral side. Ligamentous stability is evaluated using the Lachman test, anterior and posterior drawer tests, medial and lateral joint opening, the posterior sag at 70°, prone external rotation at 30 and 70, and the pivot and reverse pivot shift tests. Patellofemoral, medial, and lateral compartment crepitation are also evaluated. Tenderness, irritation, or numbness at the autograft harvest site is evaluated postoperatively. Finally, the single leg hop test is used to evaluate function compared with the unaffected side. The subjective section of the IKDC asks patients to describe and rate their knee-related symptoms (e.g., pain frequency and severity, stiffness, swelling, and sensations of knee giving away), participation in sporting activities, and knee function during daily activities and sports. The IKDC form is often accompanied by patient-reported outcome measures such as the Knee injury and Osteoarthritis Outcome Score or the Western Ontario and McMaster Universities Arthritis Index to evaluate stiffness, pain, perceived function, and quality of life.

Imaging

Clinical examination alone often cannot provide a definitive diagnosis. A full-knee radiographic knee series (weight-bearing anteroposterior, posteroanterior flexion [Rosenberg], lateral, Merchant, or skyline views) should be obtained, including 3-foot weight-bearing alignment films, to evaluate mechanical alignment of the lower limb and appreciate the severity of any varus or valgus deformities (Fig. 6). Rosenberg and Merchant views are often unremarkable; however, they can evaluate joint space narrowing, calcification of cartilage, presence of osteophytes, patellar tracking and tilt, varus and valgus malalignment, fractures, and presence of loose bodies. Malalignment can negatively affect the outcomes of cartilage procedures, accounting for over half (56%) of all failures[12]. Malalignment greater than 3° to 5° should be considered for concomitant procedures such as osteotomy. Alignment correction procedures can redistribute the weight-bearing forces across the knee and offload the damaged cartilage defect to slow the progression of OA. In patients with varus deformities, osteotomy can aid in restoring the mechanical axis of the lower limb. Lower limb alignment should be measured using the hip-knee-ankle angle (HKAA). HKAA is defined as the angle between the mechanical axis of the tibia and femur[12]. Normal lower limb alignment is between 1° and 1.5° varus[13] (Fig. 1).

Magnetic resonance imaging (MRI) is the modality of choice to evaluate the depth, size, and location of chondral defects, as well as subchondral bone quality and any concomitant ligamentous and meniscal pathologies (Fig. 2). A 1.5T MRI with T1-weighted and T2-weighted sequences has a reported sensitivity, specificity, and accuracy of up to 65.7%, 100%, and 90.5%, respectively, for cartilage defects of the knee[14]. While 1.5T MRI produces sufficient clinical evidence, 3.0T MRI has demonstrated improved visualization of cartilage pathology and stronger sensitivity in asymptomatic knees[15].

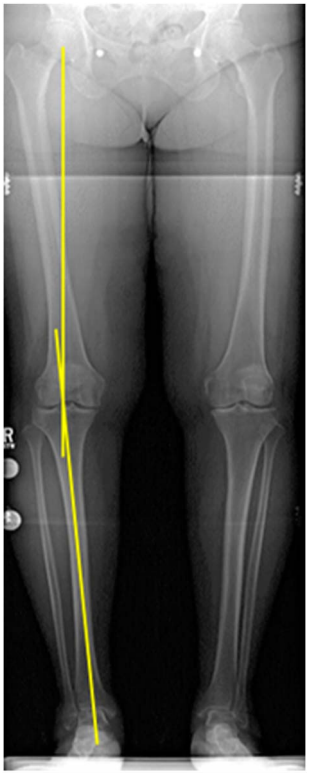

Fig. 1
Three-foot weight-bearing alignment films displaying hip knee ankle axis lines demonstrating varus malalignment.

Emerging CT-based and MRI-based 3D reconstruction techniques have provided clinicians with comprehensive bone and cartilage metrics to evaluate joint disease[16]. 3D spoiled gradient echo MRI sequences with fat suppression depict a more accurate image of cartilage defects with high contrast between the bone-cartilage and cartilage synovial fluid interfaces[16]. This allows for improved subregion analysis and an improved accuracy in measuring cartilage

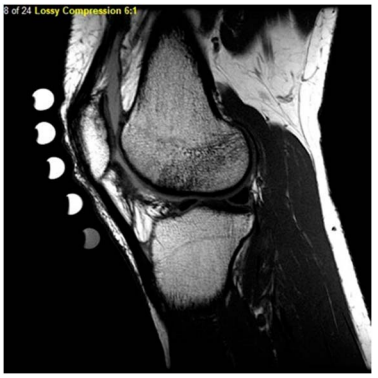

Fig. 2
Sagittal magnetic resonance image of a left knee lateral femoral condyle articular cartilage defect in a 32-year-old woman.

thickness and improved delineation of the cartilage defect[16].

Classification of Articular Cartilage and Bone Defects

Lesions are typically defined by defect size and severity, with common size cutoffs cited in the literature (small, <2 cm^2; medium, 2 cm^2 to 5 cm^2; and large, >5 cm^2)[17]. There are several intraoperative classification systems to grade severity of chondral defects, including the Outerbridge arthroscopic system and the International Cartilage Repair Society (ICRS) classification system[18,19]. The Outerbridge system is graded on a scale of 0 to 4, with 0 representing normal articular cartilage and 4 representing full-thickness chondral defects, exposed subchondral bone, and reactive bone changes[19] (Table I). The ICRS classification system also grades osteochondral defects intraoperatively on a zero to 4 scale, with zero indicating intact cartilage and 4 indicating a full-thickness cartilage defect, including the subchondral bone plate[20] (Table II).

Nonoperative Management

Conservative management is the primary treatment for all chondral defects. Pharmacologic agents can be prescribed to target patient symptoms, including topical anti-inflammatory medication (e.g., diclofenac sodium gel), systemic analgesics, and nonsteroidal anti-inflammatories (e.g., COX-2 inhibitors). Intra-articular injections including platelet-rich plasma (PRP), corticosteroids, and hyaluronic acid (HA) can also be considered. Leukocyte-rich PRP, an autologous blood-derived product, can provide functional improvement and pain relief for up to 6 months[21]. Corticosteroid injections, commonly betamethasone, methylprednisolone, or triamcinolone, provide short-term pain relief and reduction in soft tissue inflammation; however, studies have shown reduced efficacy over time[22]. Viscosupplementation with high molecular weight HA, a component of normal synovial fluid, may also be considered as a long-term alternative due to its excellent safety profile[22].

Nonpharmacological options include weight loss, unloader bracing, and physical therapy (PT)[22]. Supervised PT should be trialed for a minimum of 3 months before considering any surgical intervention. A PT program should consist of core, gluteus, and quadriceps strengthening and functional movement retraining. Utilization of an unloader brace helps shift the weight-bearing zone away from the damaged cartilage to reduce the contact stresses. A 2023 study demonstrated that patients with varus or valgus malalignment and unicompartmental osteoarthritis who wore an unloader brace for an average of 14 weeks (range 11 to 19 weeks) demonstrated a significant reduction in pain, improvement in function, improved collagen and proteoglycan concentration, and reduced cartilage edema[23]. Despite the widespread recommendation for conservative management, only 61% of patients with focal lesions demonstrate significant improvement[7].

Operative Management

When conservative management fails, surgical intervention should be considered. The appropriate surgical technique is dependent on the size and depth of the defect, the status of the subchondral bone, containment of the lesion, and lower limb alignment. Surgical treatment is usually reserved for grade 3 or 4 defects, but grade 2 defects may be treated with chondroplasty or bone marrow stimulation when found incidentally during arthroscopy[7]. Surgical treatment options can be delineated based on small (<2 cm^2), medium (2 to 5 cm^2), and large (>5 cm^2) defects. An algorithm for surgical intervention is presented in Fig. 3.

Small Defects (<2 cm^2)

Small defects can be treated with arthroscopic chondroplasty, bone marrow stimulation, or osteochondral autologous transfer (OAT).

Arthroscopic Chondroplasty

Arthroscopic chondroplasty is the most common cartilage procedure performed, accounting for >70% of all cartilage surgeries[24]. Damaged or loose cartilage is debrided back to a stable edge to alleviate mechanical symptoms and irritation without disruption of the subchondral bone. This procedure is relatively inexpensive, allows immediate weight-bearing, and demonstrates short-term improvements in pain and function, with 67% of athletes returning to preinjury levels[24]. Smaller, grade 2 defects are associated with better outcomes[24]. The removal of articular cartilage in larger,

TABLE I Outerbridge Classification System

Grade	Description
0	Normal articular cartilage
1	Focally increased signal intensity without visible cartilage loss or defect
2	Fraying of the articular cartilage surface
3	Partial thickness articular cartilage defects
4	Full-thickness chondral defects with exposed subchondral bone and reactive bone changes

TABLE II International Cartilage Repair Society (ICRS) Classification Grading System

Grade	Description
0	Intact cartilage
1	Superficial cartilage lesions
	a) Soft indentation
	b) Superficial fissures and cracks
2	Cartilage lesions project to within 50% of cartilage depth
3	Cartilage lesions exceed >50% of cartilage depth, potentially reaching the calcified layer
	a) Defect >50% but not reaching calcified layer
	b) Reaching the calcified layer
	c) Reaching (but not through) the subchondral bone plate
	d) Defect >50% with blisters
4	Full-thickness cartilage defect
	a) Defect includes the superficial subchondral bone plate
	b) Defect projects to deep subchondral bone

grade 3 to 4 defects may hasten degeneration to OA, requiring subsequent surgery in up to 12% of cases within 1 year[22,24,25]. Therefore, alternative procedures should be considered for small grade 3 to 4 defects[26].

Bone Marrow Stimulation

Bone marrow stimulation, or microfracture, involves making small perforations in the subchondral bone to create channels to release bone marrow. Mesenchymal stem cells (MSC), platelets, and growth factors are recruited from the marrow to clot the defect and produce cartilage filling (Figs. 4-A and 4-B). Microfracture can treat grade 2 lesions, but is typically indicated for small, contained grade 3 to 4 lesions[27]. Significant improvements in pain and function have been reported for up to 5 years in patients with grade 2 to 4 lesions, with return to preinjury level of sport at mean 9 months[27,28]. However, higher rates of failure and reoperation have been reported (14.7% at 2 years) following microfracture compared with OATs (8.82%)[25] and third-generation autologous chondrocyte implantation (ACI)[25,29]. Another concern is that microfracture may negatively influence the outcome of subsequent cartilage procedures. A recent systematic review and meta-analysis reported higher failure rates after ACI when patients were treated previously with microfracture compared with primary ACI alone[30].

The literature cautions against microfracture for larger defects as the replacement cartilage is structurally

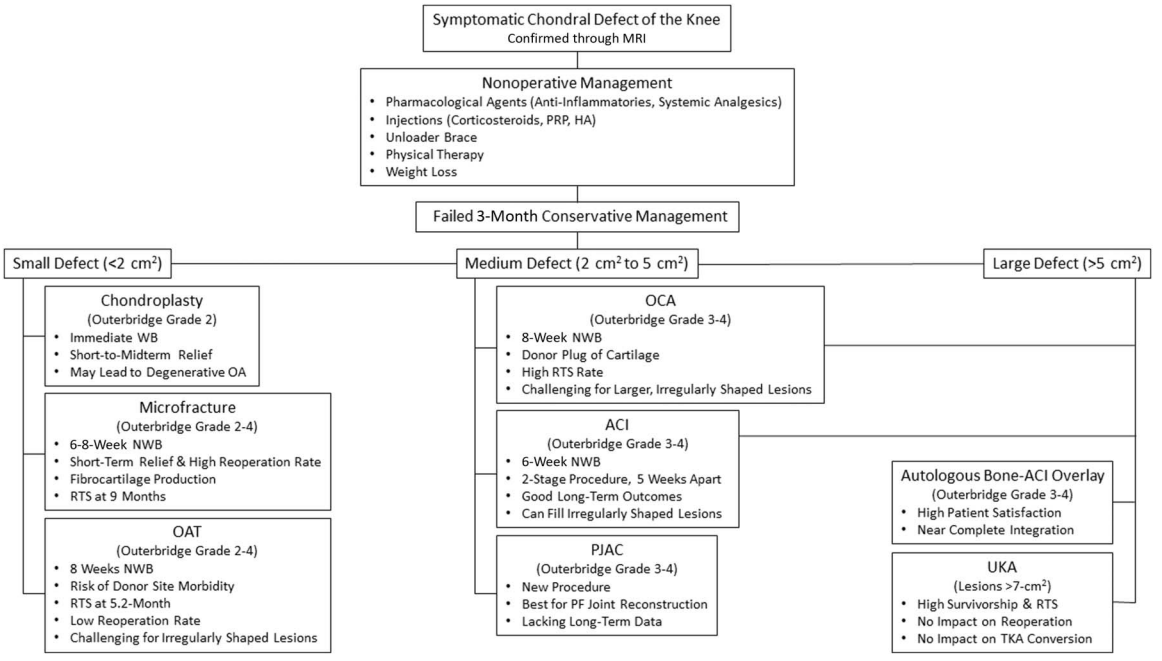

Fig. 3

A treatment algorithm for articular cartilage defects of the knee. OAT = osteochondral autologous transfer; OCA = osteochondral allograft transplant; ACI = autologous chondrocyte implantation; PJAC = particulated juvenile allograft cartilage; MRI = magnetic resonance imaging; PRP = platelet-rich plasma; HA = hyaluronic acid; NWB = non–weight-bearing; OA = osteoarthritis; RTS = return to sport; UKA = unicompartmental knee arthroplasty.

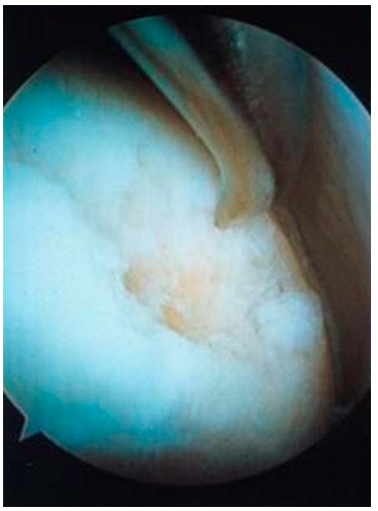

Fig. 4-A

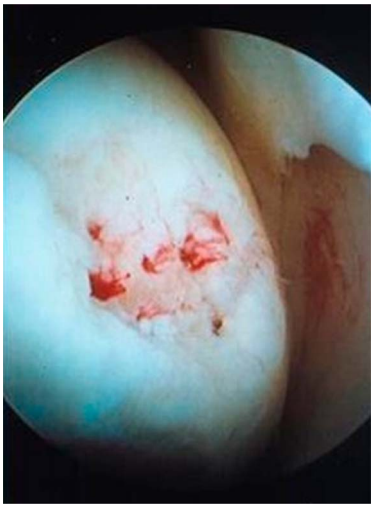

Fig. 4-B

Fig. 4 Microfracture of a femoral condyle defect. **Fig. 4-A** Perforations in the subchondral bone are made with an arthroscopic awl. **Fig. 4-B** Subsequent bone marrow extravasation which will form a clot and grow fibrocartilage.

weaker fibrocartilage in comparison with native hyaline cartilage[6]. Microfracture plus (i.e., augmented microfracture), which combines marrow stimulation with orthobiologic injections or scaffold augmentation, is effective for grade 3 to 4 lesions with similar outcomes to microfracture alone, but superior MRI Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scores[6,31,32].

Newer microfracture techniques and tools have yielded improved clinical outcomes and better repair of cartilage defects. Subchondral drilling performed with a nanopick provides deeper access to bone and greater stimulation of bone marrow cells than traditional microfracture techniques. This results in less damage to subchondral bone plate and disrupts less of the articular surface. Recent evidence shows that microdrilling (9 mm with nanopick vs. 2 mm with standard microfracture techniques) leads to improved bone fill and tissue repair with significantly lower reoperation rates. More longer term studies are required to support the efficacy of augmented microfracture techniques and microdrilling.

Osteochondral Autologous Transfer

OAT occurs in a cylindrical graft of hyaline cartilage with underlying subchondral bone harvested from a non–weight-bearing region of the knee to fill in the chondral defect. The graft harvest site should have a similar curvature and thickness to the defect to minimize surface disruption. OATs are rarely indicated for superficial grade 2 defects. Grafts are 6 to 10 mm in diameter and are press-fit into the lesion. Five-year complication rates are reported to be low (13%) with high satisfaction (81.8%) in patients with focal grade 3 to 4 defects[35]. OATs result in the highest return-to-sport rate (93% at 2 years) compared with other procedures with mean return to play at 5.2 months[28]. Despite promising short-term success, the overall reoperation rate is 28% at 10 years[25].

Medium Defects (2 to 5 cm^2)

Surgical interventions for grade 3 to 4 defects $\geq$2 cm^2 include osteochondral allograft transplantation (OCA), mosaicplasty, ACI, particulated juvenile allograft cartilage (PJAC), and osteotomy.

Osteochondral Allograft Transplantation

OCA offers treatment for larger grade 3 to 4 defects through a press-fit plug of donor articular cartilage and subchondral bone up to 16 cm^2 (Fig. 5). OCA has the advantage of an immediate structural surface of mature hyaline cartilage but requires a significant period of non–weight-bearing postoperatively to allow for donor and host bone integration. Similar to OATs, the OCA graft must follow the original contour of the cartilage to create a smooth surface. Modern screening and handling practices have

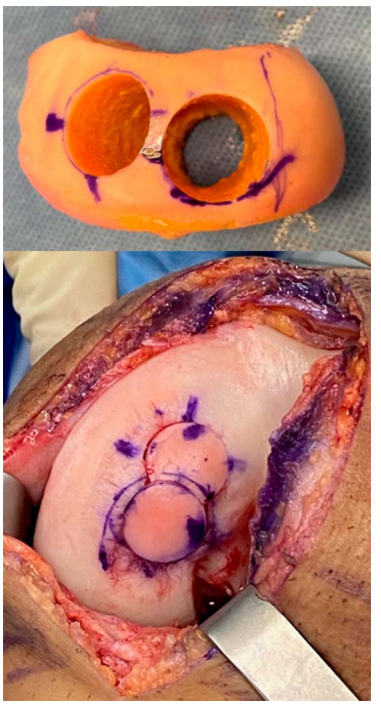

Fig. 5
Osteochondral allograft transfer, showing a donor condyle with 2 plugs excised to fit the lesion.

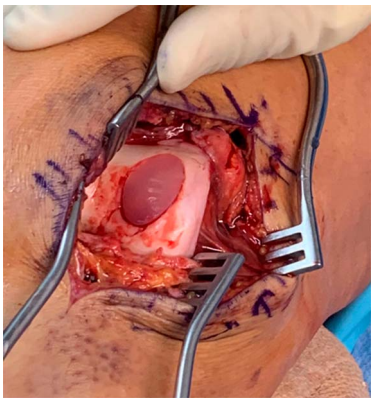

Fig. 6
Autologous chondrocyte implantation of the knee with collagen membrane in place covering defect.

made allograft disease transmission and immunogenic graft rejection extremely rare[36]. There are several reports of long-term pain reduction and functional improvement up to 12 years, with 75% return to sport rate but a 25% failure rate[37]. Risk factors for OCA failure include bipolar chondral defects, older age, higher body mass index and male sex[38]. For larger, irregularly shaped lesions, multiple plugs (i.e., mosaicplasty) can be used (Fig. 5). However, it may be difficult to contour match multiple plugs to create a congruent surface[35].

Autologous Chondrocyte Implantation

ACI is a 2-stage procedure in which chondrocytes are harvested from healthy cartilage during arthroscopy, cultured onto biodegradable collagen membranes, and implanted back into the defect 3 to 5 weeks later[2] (Fig. 6). ACI is indicated for larger, grade 3 to 4 lesions, yielding significant improvements for patients with lesions as large as 14 cm^2 and 12 mm deep into subchondral bone[2]. Significant improvements in function and pain following ACI are evident at short-term (85% return to recreational activities, 66% return to sport at 2 years) and long-term follow-up (stable clinical improvements with a 10% failure rate at 11 years)[39,40]. However, patient expectations must be managed as ACI requires 2 surgeries and 6 weeks non–weight-bearing postoperatively[2].

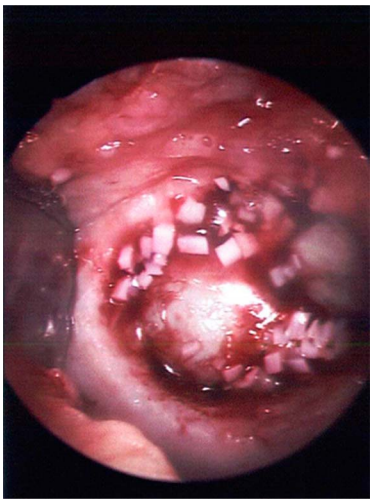

Fig. 7
Particulated juvenile allograft cartilage, used in this case to fill around the edges of a large osteochondral allograft repair of the left knee lateral femoral condyle.

Third-generation ACI, also known as matrix-induced ACI, utilizes a synthetic membrane that supports chondrocyte migration[41]. Matrix-induced ACI seeds the chondrocytes on a biodegradable type I/III collagen membrane. The graft is then sealed and fixed to the defect with fibrin glue[42]. Newer generations of matrix-induced ACI procedures are composed of an autologous chondrocyte and allogenic cartilage extracellular matrix 3D scaffold[42]. Third-generation matrix-induced ACI has demonstrated significant improvement in patient satisfaction and in patient-reported functional outcomes[41]. Newer generations of matrix-induced ACI (e.g., 3-D scaffolds) have demonstrated improvements in functional outcomes through 5 years postoperatively[42]. There are currently several other ongoing clinical trials investigating the use of 3D matrix-induced ACI[43].

Particulated Juvenile Allograft Cartilage

PJAC is a graft of fresh, minced cartilage allograft live cells from juvenile donors which is held in place with fibrin (Fig. 7). PJAC can be performed as a single-stage surgical procedure. The damaged cartilage layer is removed and replaced with a fresh graft, which is held in place with fibrin glue. Juvenile cartilage has demonstrated proliferative potential due to immature chondrocytes, yielding rapid results and excellent defect filling in MRI analysis for large, grade 3 to 4 patellofemoral and tibiofemoral lesions[6,44]. Improvements in pain and function have been reported up to 2 years postoperatively, but revision rates have been reported to be as high as 50%[45]. The use of PJAC in patellar defects is promising, with 78% of patients having majority defect fill and 67% having normal/near normal cartilage on MRI at minimum 6 months[46]. Although PJAC is perceived to be cost-effective compared with conservative treatment and other surgical treatments, more reports of long-term outcomes are needed to determine its true efficacy[47]. A recent case report with 11-year follow-up showed a MOCART score of 80 and complete surface congruity on arthroscopy[48].

Osteotomy

High tibial or distal femoral osteotomy (HTO or DFO), in conjunction with other cartilage repair procedures, may be considered when a malalignment is present[49]. HTO is indicated for the treatment of varus deformity and medial compartment defects, whereas DFO is indicated for valgus deformity and lateral compartment defects[50,51]. HTO and DFO can minimize contact pressure on the implanted graft, reduce the load on the degenerated knee compartment, and aid in restoring knee biomechanics[49]. Reoperation rates range from 10.5% to 19.5%, which is 30% to 50% lower than that for ACI and OATs alone[49].

Concomitant tibial tubercle osteotomy (TTO) and ACI are another promising intervention for patellofemoral chondral defects[52]. TTO repositions the tibial tubercle to aid in improved patellar tracking and reduction in the load on the medial or lateral patellar facet to reduce pain and improve function[53]. In a highly active military population, concomitant TTO and ACI significantly improved pain and returned 78% of patients to active duty with a low failure rate (4.1%)[52].

Large Defects (>5 cm²)

Large defects may be treated with OCAs, ACI, or a combination "sandwich" treatment (autologous bone graft with ACI overlay)[54]. Patients with larger lesions have greater improvements in outcome scores compared with patients with lesions <5 cm^2 following OCA at minimum 2 years[37] and sustained functional outcomes following ACI at 10 years[40]. Autologous bone-ACI overlay is a technique in which autologous bone grafting and ACI are performed simultaneously[54]. Cultured chondrocytes are taken from the autologous bone graft site and marrow space[54]. The culture chondrocytes are then placed between 2 periosteal or collagen membranes, forming a "sandwich". The "sandwich" is positioned on the surface for single-stage reconstruction of the osteochondral unit[54]. There are 2 "sandwich" types: ACI "full-sandwich" and ACI "segmental sandwich". In the "full-sandwich" technique, the ACI cartilage repair covers the entire area of bone grafted. In the "segmental sandwich" technique, the bone graft covers only a portion of the entire defect area treated with ACI. Autologous bone-ACI overlay yields high patient-reported satisfaction and complete/near-complete defect filling/integration on MRI[54]. For lesions >7 cm^2, a unicompartmental knee arthroplasty is a good alternative that does not affect future outcomes of reoperation or conversion to total knee arthroplasty, with high survivorship and return to sport in 100% of patients aged younger than 60 years[55].

Postoperative Rehabilitation

PT should be initiated within the first week postoperatively[56]. Guided ROM exercises are encouraged to promote healing and prevent stiffness[56]. Cryotherapy may be used to reduce edema, effusion, and pain[57]. Weight-bearing is initially limited during the first 3 to 5 days but permitted as tolerated after chondroplasty[58]. OAT and OCA provide a mature cartilage surface and are generally held non–weight-bearing for 3 weeks, followed by progression to limited weight-bearing while locked in extension, and finally full–weight-bearing at 6 weeks[56,59]. Microfracture, matrix-induced ACI, and PJAC techniques do not provide a mature cartilage surface and are generally non–weight-bearing for 6 weeks with a return to full activity projected at 9 to 12 months[6].

Complications

In general, cartilage repair procedures are relatively safe with minimal complications. Patient selection is important when considering surgical intervention. Younger patients with lower BMI, fewer prior knee surgeries, and less time between injury and surgery have fewer complications[24]. Infection is always a concern with any surgical procedure. Reported surgical site infections are low after cartilage repair procedures, ranging from 0% after PJAC to 0.9% to 1.8% after OCA[60-62]. Smoking may increase risk of infection, as well as, poor healing. Graft hypertrophy is the most common complication requiring revision arthroscopic repair and contributes to 1-year reoperation rates of 5%[25,63]. Graft failure requiring reoperation is also common, with 2-year reoperation rates up to 10.1% for OATs, 13.6% for OCA, and 29.7% for ACI[25]. Risk factors for failure after ACI include female sex, defect size (9.1 ± 4.9 cm^2), and hypertension[64]. Therefore, patient selection is key when selecting the appropriate procedure. Microfracture has the highest risk of conversion to arthroplasty at 2 years (6.7%) compared with OATs, OCA, and ACI[25]. Failure following cartilage repair can also be due to uncorrected malalignment (up to 56% of cases), untreated meniscal pathology (19%), and ligamentous instability (5%)[12].

Emerging Technologies

New alternatives, including stem-cell injection-based therapies, as well as scaffolds derived from biomaterials such as coral, are currently being investigated for their use in the treatment of chondral or osteochondral defects[65]. MSCs can be harvested from bone marrow (e.g., autologous matrix-induced chondrogenesis and bone marrow aspirate concentrate), from donor tissue (e.g., human umbilical cord blood-derived MSCs and viable cartilage allograft putty), or from autologous adipose tissue[65]. Cells are injected into the joint space or embedded within a collagen scaffold, much like ACI procedures. New, prefabricated, biocompatible, and bioresorbable scaffolds, such as aragonite biphasic osteochondral scaffolds derived from coral or cryopreserved viable osteochondral allografts from human cadavers, are being investigated as accessible alternatives to more costly procedures[65]. MSCs differentiate into chondrocytes and induce chondroprogenitors, growth factors, and ECM proteins to halt cartilage degradation, reduce inflammation, and create a reparative environment[66]. Histological studies suggest that the new cartilage structure closely resembles hyaline cartilage in a model of MSC-injected rats with a created patellofemoral focal cartilage defect[67]. Early subjective results of pain reduction and improved knee function have been reported[65-67]. The use of MSCs in clinical trials is becoming increasingly prominent[68]; however, stem-cell therapies are still considered experimental by the Food and Drug Administration[69]. Further research is needed to support their efficacy.

PRP, bone-derived MSCs, and adipose-derived MSCs in conjunction with microfracture are promising alternatives to restore knee function[70-72]. Combined intra-articular injections of bone-derived MSCs with PRP and adipose-derived stem cells with PRP have led to improved pain, functional outcomes, and a reduction in inflammatory cytokines by 6 to 12 months[70,71]. Similar results have been seen with microfracture followed by a combined PRP and adipose-derived MSC injection[72]. In addition, second look arthroscopies have found a solid, smooth cartilage

layer with an adequate cell population, closely resembling native tissue[72].

Summary

Focal knee articular cartilage defects are a challenging disease entity due to poor vascularity and limited regenerative capacity resulting in pain, stiffness, and physical limitations. Conservative management including PT, unloader braces, anti-inflammatories, or corticosteroid injections are the recommended first-line treatment. If conservative treatment fails, surgical treatments may relieve symptoms and delay arthroplasty. Careful patient selection including defect size and severity dictates the choice of treatment. Outerbridge grade 2 defects may be treated with chondroplasty, regardless of size. Grade 3 to 4 defects <2 cm^2 are best treated with microfracture or OATs. Grade 3 to 4 defects 2 to 5 cm^2 are treated with OCA, ACI, or PJAC. Larger defects >5 cm^2 may be treated with OCA, ACI, or OCA-ACI overlay. New technologies including prefabricated scaffolds, biologics, and MSCs will expand our treatment options for focal cartilage defects of the knee.

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