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A Treatment Approach for Articular Cartilage Defects

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Abstract

Osteoarthritis is one of the most common disease affecting older adults, and can have a drastic impact on quality of life. This degenerative cartilage disease can often be the result of progression of focal cartilage defects. Fortunately, a plethora of treatment options, both surgical and non-surgical, exist for focal articular cartilage defects. However, because the natural history, incidence, and patient demographics of focal articular cartilage defects are not fully defined, it is important to treat these defects on a patient-specific level. Clinicians must integrate many features, including patient-specific goals, risk factors for disease progression, symptoms, lesion characteristics, comorbidities, and responsiveness to conservative treatment in a patient-centered clinical encounter before being able to decide if surgery is indicated and, if so, the optimal surgical management for the patient.
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Key Words: articular Cartilage defect, Osteoarthritis, natural history

Background:

Articular cartilage disease, namely osteoarthritis, is the most common joint disease in the world affecting 80% of patients >75 years old [1]. The progression of this disease generally begins with focal cartilage lesions. In a prospective study of 65 patients with a mean age of 62.7 years old, Carnes et al demonstrated that the presence of cartilage defects was shown to independently predict eventual cartilage volume loss and risk of future knee replacement [2]. However, the majority of articular cartilage lesions remained stable with little regression after 2.9 years. In those patients whose defects demonstrated progressive degeneration, baseline risk factors included radiographic evidence of osteoarthritis, tibia size, higher body mass index, and female sex. These factors are important to consider when determining approach to treatment.

Given the risk of cartilage volume loss and correlation with future knee replacement, it is important to consider articular cartilage injuries in younger populations. These injuries commonly occur in young, active patients and generally occur after direct trauma, often in conjunction with other injuries, such as ligamentous or meniscal injuries [3]. These injuries can also arise from degenerative patterns or, less commonly, from metabolic disorders of subchondral bone such as osteonecrosis or osteochondritis dissecans. The treatment of focal articular cartilage disease presents a challenge to physicians because the variability in patient presentation and symptoms makes it difficult to determine the appropriate type and timing of treatment for each patient.

While the incidence and patient demographics of cartilage lesions are not fully documented, full-thickness lesions are more common in athletes than in the general population. In a systematic review by Flanigan et al looking at 931 athletes, 36% were found to have full-thickness lesions on MRI, but only 14% of these lesions presented with associated symptoms [3]. These results highlight an important concept in the management of articular cartilage lesions: treatment must be tailored to address symptoms, not imaging findings.

As the number of treatment options for articular cartilage defects expands,

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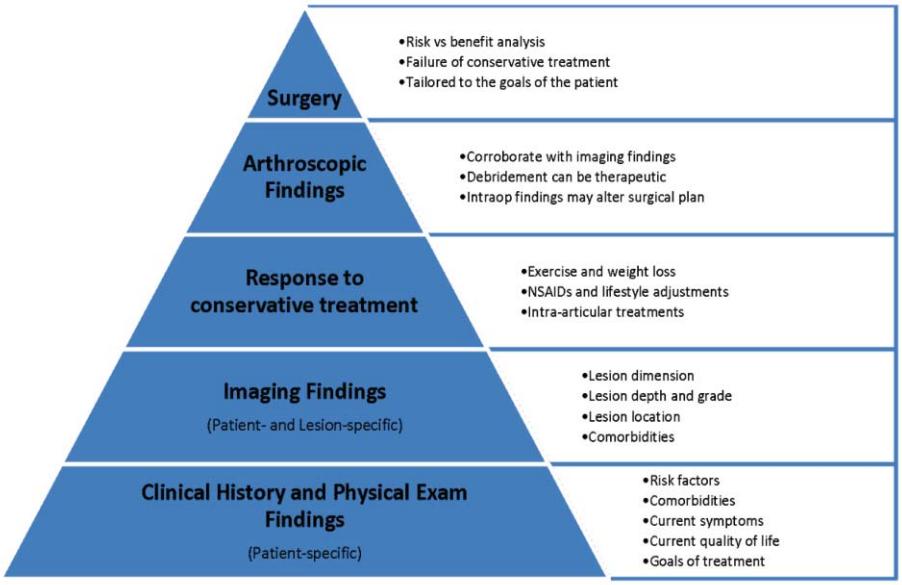

Figure 1: The decision to send a patient to surgery is the endpoint of a heirarchy of decision making. The appropriate information must be gathered from each step of the process to ensure optimal patient outcomes. Surgical interventions should always be the last step of the equation.

evidence-based, patient-centered decision-making is required to provide the best possible outcomes to patients (Fig. 1). Unique patient concerns, expectations and goals must be addressed in the treatment discussion. By managing patient expectations to arrive at a mutually agreed upon and achievable goal, physicians can maximize patient satisfaction.

The purpose of this article is to present a systematic approach to decision-making in treating articular cartilage injury and to provide a brief summary of the currently available and up-and-coming treatment options.

Patient-Centered Evaluation

Clinical History: A key to decision-making in the treatment of articular cartilage lesions is the patient-centered evaluation. The past medical history can contribute significantly to the management plan.

Comorbidities, either systemic or joint-specific, previous surgical history, and current medication regimen can impact prognosis and outcome. A thorough history and physical is necessary to elicit patient demographics that influence disease progression and patient outcomes (age, body mass index, sex, malalignment, and smoking status) [2]. Specifically, age has been shown to be predictive of positive outcomes in patients <30 years old [5-7]. However, this should not disqualify older patients from these procedures given the possibility of restoring or prolonging function and delaying the need for a total knee arthroplasty. The clinical history should also include discussion of timing (acute versus chronic), injury mechanism (twisting, fall, or insidious onset), and any concomitant injuries, specifically meniscal or ligamentous injuries.

Articular cartilage injury typically presents as pain localized to a single compartment that is worse with load-bearing and correlates with a defect found on imaging or diagnostic arthroscopy. However, patient presentation can range widely, sometimes even presenting solely as painless joint swelling during activity. It is important to note that symptoms do not reliably correlate with degree of damage, including the size or grade of a lesion [8]. As such, the presence and nature of the patient's symptoms and their impact on the patient, rather than objective lesion-specific findings, should drive treatment decisions. The type and severity of symptoms (clicking, locking, or swelling), magnitude and quality of pain, and any complaints of instability and loss of function should all be elicited. Exacerbating factors and activities that the patient can no longer effectively or comfortably perform should also be explored. In addition, one should always inquire about pain at rest. Rest pain is unpredictably related to intra-articular pathology and must be approached with caution to manage patient expectations of cartilage surgery resolving this type of pain.

Physical examination: The role of the physical examination in guiding treatment decisions is to confirm that the patient's symptoms are attributable to the cartilage defect and to detect any comorbidities. It is critical to evaluate gait and gross musculoskeletal deformities to develop a holistic assessment of a patient's functional abilities and deficiencies. Specifically, axial malalignment or rotational abnormalities must be identified and addressed. These conditions can increase forces through the affected compartment and may need to be corrected prior to cartilage restoration to ensure a successful outcome.

Strength and flexibility in both lower extremities should be examined to compare the injured extremity with the healthy, contralateral side. Specifically, the examiner should look for signs of weakness resulting from compensatory

mechanics. Additionally, any effusions or limitations in movement or range of motion can reflect the extent of pathology and provide clues on the potential efficacy of specific treatments.

Concomitant Knee Pathologies:

It is important to evaluate for concomitant knee pathologies during both the clinical history and the physical examination. Joint-specific comorbidities such as ligamentous or meniscal injury and tibiofemoral or patellofemoral malalignment can influence treatment outcomes. These conditions must be addressed in a comprehensive treatment strategy to ensure optimal outcomes. Sometimes additional surgeries may be required – either in a stepwise progression or concurrently.

Imaging: Imaging is an essential adjunct to the clinical history and physical exam for diagnosis and management. Plain radiographs have a key role in a patient's evaluation. In both acute and chronic pathologies, weight-bearing anterior-posterior and flexion posterior-anterior radiographs can be used to assess the severity of osteoarthritis [9]. Importantly, severe osteoarthritis is a contraindication to cartilage restoration surgery. Merchant and lateral views of the patellofemoral joint can be enlightening in cases with anterior knee pain worsened by jumping or squatting, but these views can underestimate the extent of cartilage damage. Standing full-length radiographs should be used to assess for malalignment.

While radiographs can help evaluate advanced disease, they have a lower sensitivity for focal defects. In symptomatic patients with normal weight-bearing radiographs, MRI plays a crucial role in assessing for comorbidities, such as meniscal or ligamentous injury, and in evaluating subchondral bone for areas of edema, osteochondritis dissecans, avascular necrosis, or fractures. Additionally, rapid identification, sizing, and characterization of focal chondral lesions can be obtained via 2-dimensional fat suppression and 3-dimensional fast-spin echo sequences. Furthermore, gadolinium contrast sequences can determine the quality of cartilage with regards to proteoglycan content.

Despite advancements in imaging technology, arthroscopy remains the gold standard in the diagnosis of cartilage lesions. It is important to counsel patients that arthroscopy with debridement can be both a diagnostic and therapeutic procedure, potentially delaying the need for other surgical treatment. An index arthroscopy can be indicated to evaluate the meniscus, ligaments and intra-articular cartilage if current information is dated or incomplete. Arthroscopy can assess for relevant bipolar disease and provide grading of defects by Outerbridge criteria [10]. As a note, the International Cartilage Repair Society has provided updates to the Outerbridge criteria in their own scoring metric [11].

Lesion Characteristics: The of symptomatic cartilage lesions is determined in part by lesion depth and dimension. Guettler et al showed that lesions >1cm in diameter can lead to deteriorating symptoms [12].

Indications for procedures depend on absolute area. Microfracture and osteochondral autograft transplant surgery (OATS) are recommended for smaller defects (<2.5cm2) and autologous chondrocyte implantation (ACI) and osteochondral allografts (OCA) are recommended for larger (>4cm2) defects [13]. It is important to evaluate for lesion depth during arthroscopy because full-thickness chondral lesions (those extending to the subchondral bone) require restorative treatment options – such as OCA. Defect location also plays an important role in management. There are a greater number of treatment options (microfracture, scaffolds, ACI, OCA or OATS) available for condylar defects. Conversely, the patellofemoral joint has much more limited treatment options because it is difficult to match topographically for grafting. Therefore, larger patellofemoral defects are more commonly addressed using surface treatments. Tibial defects also have geometric considerations, and because they are difficult to access and have a lack of evidence available to guide treatment, our approach is to start by correcting meniscal problems, malalignment, and femoral condylar defects as first-line treatment.

Goals of treatment:

A tenant of treatment for cartilage defects is to avoid treating radiographic or arthroscopic findings if they do not match patient symptoms. To maximize patient satisfaction, treatment decisions must be made in an effort to address symptoms and after an extensive, patient-centric discussion of risks versus benefit. "Prophylactic treatment" with the goal of preventing disease progression or the future development of symptoms in the absence of current symptoms is discouraged because the natural history and progression of articular cartilage lesions is unpredictable, and thus the outcomes of treating asymptomatic lesions is also unpredictable. In deciding to treat a patient, it is important to focus on individual performance demands – such as return to work or sport. The goals of therapy should vary according to age group and level of baseline (and desired) function (e.g. a teenager with osteochondritis dissecans vs an in-season professional athlete). If the goals of treatment are to return to activities more intense that those required of daily

living, this can tip the scales in favor of an operative approach as there is a lower likelihood that initial conservative management will be sufficient. Thoughtful communication between the provider and patient, focusing on functional limitations and specific goals of therapy, allows for mutual understanding and the alignment of provider and patient goals of care.

Nonsurgical care:

Nonsurgical care is an important pillar of treatment for articular cartilage defects and should be discussed as an option prior to surgical intervention [14, 15]. Physical therapy and exercise can provide effective symptom relief and longer-lasting relief, and are often used to complement other interventions in younger, more active patients [16]. While the nature of articular cartilage disease often causes patients to become more symptomatic with increasing activity, there is not sufficient evidence that activity results in pathoanatomical changes such as increased cartilage damage or osteoarthritis progression [17]. Thus, while activity should be restricted in patients on an individualized basis, in general, patients should be counseled that benefits of exercise outweigh any negative effects. A significant benefit of exercise is the potential for weight loss. Obesity is highly associated with symptomatic osteoarthritis, and overweight patients should be counseled to lose weight in addition to other interventional measures.

In addition to exercise, weight loss, and non-steroidal anti-inflammatories, another option for nonsurgical treatment is intra-articular injections of corticosteroids, viscosupplementation, and biologics (platelet-rich plasma, amniotic suspension allografts, and bone marrow aspirate concentrate). Intra-articular steroids are widely accepted and simple to use, but have a short-lived clinical benefit of 1-6 weeks with little evidence that benefits remain 6 months after treatment. Conversely, viscosupplementation with hyaluronic acid provides longer improved function (24-26 weeks) with consistent benefits across many different groups of patients regardless of amount of baseline synovial fluid [18, 19]. The mechanism of action is likely from improving normal synovial fluid function and articular homeostasis [20, 21].

Biologic injections have shown promise for conservative treatment of articular cartilage lesions. Platelet-rich plasma (PRP) likely does not cause cartilage regrowth, but in practice it has demonstrated superior results, especially among active populations with lower grade cartilage damage [22, 23]. While PRP is a relatively expensive treatment option for patients, it has been shown to have good efficacy if used appropriately. It has been well-documented that PRP provides improved symptomatic relief compared to controls [24]. There is also evidence that PRP may stimulate the recruitment and expansion of mesenchymal stem cells, the synthesis of hyaluronic acid, and the production of extracellular matrix. In recent investigations, PRP, particularly leukocyte-poor PRP, has been show to improve symptoms up to 1 year through mostly anti-inflammatory effects [25]. Additionally, a recent prospective study demonstrated PRP to be superior to hyaluronic acid at 1 year follow-up, but both groups continue to have a number of non-responders [26]. Since a significant incidence of non-responders has been shown with both hyaluronic acid and PRP, an appropriate treatment algorithm is to trial a first injection and stop if there is no symptomatic relief. If symptomatic relief is obtained, however, the evidence supports continued treatment for up to three rounds of injections.

Another potentially promising treatment option in the realm of biologics is bone marrow aspirate concentrate (BMAC). It is easily collected and has demonstrated good chondrogenic potential, especially in conjunction with surgery. However, regulatory barriers have limited BMAC use as a conservative, intra-articular injection outside of surgery. Mixed results have been reported so far with many ongoing clinical studies [27]. Before BMAC can be used on a larger scale, more investigational trials are required, and regulatory barriers to its use outsides of an operative setting must be overcome.

Criteria for surgery:

To ensure an optimal outcome, both the patient and the provider must mutually decide that the operative threshold has been crossed. This means that the patient does not feel he or she is able to continue at the current level of pain or function and conservative options are not sufficient. Prior to deciding on surgical treatment, nonoperative management should be discussed, and the potential benefits must be weighed against the risks of surgery. Surgery may be considered as a treatment option only if it is determined that surgical treatment has a reasonable likelihood of meeting patient's and surgeon's expectations. Good surgical candidates are those who have failed conservative measures and have recent arthroscopic findings demonstrating pathoanatomy amenable to surgical treatment. In these cases, all information about patient goals and any concomitant pathologies should be considered to work with the patient and develop a cohesive surgical plan through a shared decision-making model.

Surgical Options:

Debridement should be the first line treatment for patients with small defects (<2cm2), in-season athletes or patients with lower levels of demand with new symptoms. Simple irrigation and

debridement may temporarily improve symptoms in up to 60% of patients, potentially obviating the need for more intensive operations [28-32]. In the senior author's (BJC) practice, arthroscopic evaluation and debridement are generally conducted on patients for both diagnostic (future operative planning) and therapeutic purposes. In patients planned to undergo a more intensive procedure, intraoperative arthroscopic findings may alter the surgical plan.

Marrow stimulation techniques, including microfracture, subchondral drilling, and abrasion therapy, have been shown to have some benefit in patients with moderate symptoms with smaller defects (<2cm2) or in less active patients with larger lesions. However, these techniques result in the generation of type 1 fibrocartilage and are less durable than other techniques, possibly due of the lack of type 2 collagen generation [14, 29, 33, 34]. Commercial scaffolds and biologics may show promise in augmenting these techniques [35].

Osteochondral grafting, with both allografts and autografts, has proved to be an effective technique. Osteochondral autograft transplant surgery (OATS) is a restorative procedure in which a plug of native cartilage from a non-weight-bearing region is harvested and transplanted to fill in a weight-bearing defect, generally for smaller lesions (between 1-4cm2). While OATS has some limitations, including difficulty filling large defects and donor site morbidity, a recent review has shown 72% success at 10 years with high rate of return to sport [36]. Failure of OATS can be predicted by older age, previous surgery, and larger defect size [37]. Osteochondral allografts (OCA) escape many of the limitations of OATS and have been shown to provide reliably good outcomes when treating midsized defects (2-4cm2) [38, 39]. OCA has also shown good outcomes when used as a revision procedure for previous operations, such as microfracture [40], and in pediatric applications [41]. Further applications of OCA include use in bipolar lesions with predominant pathology on one side and in defects of the patellofemoral joint; however, these applications need to be evaluated with more long-term data [42]. OCA has also shown excellent return-to-sport in high level athletes [43]. Given these characteristics, as well as good long-term survival, especially in the femoral condyle [44], OCA has been used increasingly for appropriate patients in the senior author's practice (BJC).

Autologous chondrocyte implantation (ACI), which involves harvesting a patient's own chondrocytes and culturing them for re-implantation, has demonstrated efficacy for larger lesions. It is less commonly used in femoral lesions due to a relatively high cost and increased work of treatment when compared with alternative, single-staged techniques (OATS and OCA). First generation ACI, using a periosteal patch, demonstrated the complication of patch hypertrophy, but newer patches using synthetic collagen have shown better outcomes with possibly more durability [45-48]. In the senior author's practice, this technique was primarily used in the patellofemoral joint, but even this application has been slowly phased out in favor of OCA [49]. However, long term data still needs to be developed in the field of patellofemoral cartilage defects.

Emerging treatment options in the field include a new generation of cell-based technology that can hopefully provide improved techniques for ACI. Additionally, future developments of cryopreserved osteochondral allografts and cartilage matrices offer promise in more effective restorative and regenerative treatments. Like existing cartilage treatments, these new treatments need further investigation to determine the patient-specific and lesion-specific treatment parameters that provide the best outcomes.

Conclusions

There are a plethora of surgical treatment options currently available for focal articular cartilage disease, and it is important to properly select patients to ensure optimal outcomes and patient satisfaction. Important criteria to consider before proceeding with surgical treatment of these lesions are patient-specific risk factors for disease progression, comorbidities, lesion characteristics, symptoms, treatment goals, and responsiveness to conservative treatment. Only after discussing all of these factors in a patient-centered clinical encounter can the appropriate decision be made to proceed with surgical treatment.

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