A Review Paper

The Treatment of Cartilage Defects in the Knee Joint: Microfracture, Mosaicplasty, and Autologous Chondrocyte Implantation

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Abstract

The efficacy of microfracture (MF), mosaicplasty (MO), and autologous chondrocyte implantation (ACI) techniques are still a matter of debate. This review aims to analyze comparative studies of these techniques, review the results of no treatment, and the natural history of untreated articular cartilage lesions.

A PubMed search on the topic was performed. The most important (14) articles, as judged by the author, were selected for this review.

There is limited evidence that any intervention significantly alters the natural history of these lesions and there is no evidence of significant difference between ACI and MF and MO. Paramount for successful surgical cartilage repair is a stable knee with a well-aligned lower limb. There is insufficient evidence at present to say that ACI is cost-effective, compared with MF or MO.

Treatments for managing full thickness articular cartilage defects of the knee, including microfracture (MF) and mosaicplasty (MO), are not always effective. When they are, long-term benefits may not be maintained and osteoarthritis may develop.[1,2] An alternative is autologous chondrocyte implantation (ACI), the surgical implantation of healthy cartilage cells into the damaged areas. In other words, various treatment modalities for deep cartilage defects are currently available.[3-8] The efficacy of MF, MO, and ACI techniques is still a matter of debate.

The purpose of this review was to: 1) clarify whether there is a difference between ACI, MO, and MF regarding their results; 2) review the results of no treatment and compare this control group to the treatment group (ie, what is the natural history of untreated small articular cartilage lesions?); 3) analyze the role of continuous passive motion (CPM) after the surgical treatment of cartilage defects; 4) review the role of magnetic resonance imaging (MRI) in the assessment of cartilage defects; and 5) define whether ACI is a cost-effective procedure.

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Methods

A PubMed search was performed using the following key words: cartilage lesion, knee, natural history, ACI, microfracture, mosaicplasty. The most important (14) articles, as judged by the author, were selected for this review. The main criterion for selection was that the articles addressed and provided solutions to the questions of this article.

Results

Only 14 articles were reviewed on the topic of cartilage lesions, knee, natural history, ACI, MO, and MF. Some of them were comparative studies. Other studies also analyzed the natural history of knee cartilage lesions, the role of CPM in the postoperative period of the surgical procedure, the role of the MRI, and a comparison between the cost-effectiveness of ACI, MO, and MF.

Natural History of Knee Cartilage Lesions

The natural history of cartilage lesions in the knee joint has been investigated in the literature by means of experimental and clinical studies.

Experimental Studies on Osteochondral Defects. In an experimental study on osteochondral defects, Albrecht and colleagues[3] did not find hyaline cartilage histologically in osteochondral defects left untreated. In their study, 75 knee joints in 46 adult rabbits with osteochondral defects of 4 mm diameter were placed by a drill reaching the cancellous bone. Twenty-three defects were left untreated, closed by collagen foam or fibrin adhesive, or a combination of both. Fifty-two defects were closed with very small autologous cartilage fragments and a special fibrin adhesive. In the first group of 23 joints, which were observed for up to 40 weeks, no hyaline cartilage was found histologically in any of the defects. In the second group, a rapid proliferation of chondrocytes appeared with development of hyaline cartilage with alcianblue-positive matrix. It resembled juvenile cartilage in its histologic appearance and with regard to the induction of ossification.

In another experimental study, Burks and colleagues[4] compared untreated or bone-grafted defects with osteochondral allografts. Their hypothesis was that small osteochondral autograft plug placed in the center of a large defect in a sheep femoral condyle would be superior to either an untreated or a bone-grafted defect. The main conclusion of the study was that osteochondral autograft plugs may be able to treat larger articular lesions without complete fill of the defect.

Clinical Studies on Ostechondritis Dissecans. De Smet and colleagues[5] investigated the usefulness of plain film and MRI findings in predicting the outcome of conservatively treated patients with femoral juvenile osteochondritis dissecans (JOCD). Without knowledge of the clinical outcome, they retrospectively reviewed the initial plain films and MRI examinations. The main conclusion was that it appears that a good clinical outcome is likely when the femoral growth plate is open, when the JOCD is small, and when the lesion is stable by MRI. When an articular defect is found on an MRI, the patient is likely to have a poor outcome.

According to Polousky,[6] despite our long recognition of JOCD, the natural history and most effective therapies are poorly understood. Treatment decisions must be based on the stability of the lesion. Stable JOCD lesions should be treated initially with activity modification and possibly, immobilization. Unstable lesions and stable lesions not responding to an initial course of nonoperative therapy should be surgically treated. Surgical treatment must be based on the radiographic and arthroscopic characteristics of the lesion. Multiple techniques from simple arthroscopic drilling and fixation to salvage techniques for cartilage restoration can be used.

Clinical Studies on Articular Cartilage Defects. Widuchowski and colleagues[7] stated that the potential candidates for cartilage repair surgery are patients with 1 to 3 localized Outerbridge grade III and IV cartilage lesions. However, because these patients are a heterogeneous group, and the natural history of cartilage lesions remains unknown, the total number of patients who might benefit from cartilage repair also remains unknown.

According to Safran and Seiber,[8] the complex structure and biomechanical function of articular cartilage make chondral injuries a management challenge. Articular cartilage has limited, if any, capacity to heal and/or regenerate. Although the natural history of articular cartilage lesions has not been clearly studied, significant injuries are believed to progress, resulting in degenerative arthritis of the joint. Changes have been made in surgical techniques in an attempt to better treat these lesions. However, there is limited evidence that any surgical procedure significantly alters the natural history of these lesions. Randomized trials have been done to examine the results of common restoration procedures performed today, such as MF, MO, and ACI. Because the natural history of articular cartilage lesions has not been defined, we can evaluate the utility of surgical interventions only by comparing methods.

Comparative Studies

Wasiak and colleagues[9] determined the effectiveness of ACI in people with full thickness articular cartilage defects of the knee. In their report, they included 4 randomized controlled trials. One trial of ACI versus MO showed statistically significant results for ACI at 1 year, but only in a post hoc subgroup analysis of participants with medial condylar defects; 88% had excellent or good results with ACI versus 69% with MO. A second trial of ACI versus MO showed no statistically significant difference in clinical outcomes at 2 years. There was no statistically significant difference in results at 2 years in a trial comparing ACI with MF. In addition, 1 trial of matrix-guided ACI versus MF did not have enough long-term results to reach definitive conclusions. The main conclusion of the study was that there is, at present, no evidence of significant difference between ACI, MF, and MO.

Vasiliadis and Wasiak[10] evaluated the Cochrane Bone, Joint and Muscle Trauma Group Specialized Register, the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, SPORTDiscus, the WHO International Clinical Trials Registry Platform, and Current Controlled Trials. They sought to determine the efficacy and safety of ACI in patients with full thickness articular cartilage defects of the knee. The selection criteria were randomized and quasi-randomized trials comparing ACI with any other type of treatment (eg, no treatment or placebo) for symptomatic cartilage defects of the medial or lateral femoral condyle, femoral trochlea, or patella. Six heterogeneous trials were identified. Three trials compared ACI versus mosaicplasty. One showed statistically significant results in favor of ACI at 1 year in the number of people with 'good' or 'excellent' functional results. Conversely, another trial found significant improvement for the MO group when evaluated using one functional scoring system at 2 years, but no statistically significant differences based on 2 other scoring systems. A third trial showed no difference between ACI and MO, 10 months on average after the surgery. There was no statistically significant difference in functional results at 2 years in single trials comparing ACI with MF or characterized chondrocyte implantation versus MF. The results of the sixth trial comparing matrix-guided ACI with MF were undermined by the great loss to follow-up. Vasiliadis and Wasiak[10] concluded that there is insufficient evidence to reach conclusions on the use of ACI for treating full thickness articular cartilage defects in the knee. Further good quality randomized controlled studies with long-term functional outcomes are needed, they added.

Data on clinical effectiveness was obtained by Clar and colleagues[11] from randomized trials, supplemented

by data from selected observational studies for longer term results, and for the natural history of chondral lesions. Due to a lack of long-term results such as later osteoarthritis and total knee replacement, only illustrative modeling was done, using some assumptions that seemed reasonable, but were not evidence-based. Four randomized controlled trials were included, as well as observational data from case series. Two studies compared ACI with MO, the third compared ACI with MF, and the fourth compared matrix-guided ACI (MACI) with MF. Follow-up was 1 year in 1 study and up to 3 years in the remaining 3 studies. The first trial of ACI versus MO showed that ACI gave better results than MO at 1 year. Overall, 88% had excellent or good results with ACI versus 69% with MO. About half of the biopsies after ACI showed hyaline cartilage. The second trial of ACI versus MO found little difference in clinical results at 2 years. Biopsies from the ACI group showed fibrocartilage rather than hyaline cartilage. The trial of ACI versus MF also found only small differences in outcomes at 2 years. Finally, the trial of MACI versus MF contained insufficient long-term results, but the study showed the feasibility of doing ACI by the MACI technique. It also suggested that after ACI, it takes 2 years for full-thickness cartilage to be produced.

According to Pietsch and Hofmann,[12] several treatment modalities for the osteoarthritis of the knee in middle-aged patients to preserve the joint are available. They reported good and excellent results with MF at a follow-up of 2 years. They stated that cartilage defects up to 4 cm^2 should be treated by the mosaic-type osteochondral autologous transplantation. ACI should be considered when larger defects are presented in younger patients. In existing osteoarthritis, ACI is not recommended. They concluded that up until now, there is no significant difference in results between ACI, MO, and MF. The basis for successful surgical cartilage repair is a stable knee with a well-aligned lower limb. If the lower limb is misaligned, an alignment additional osteotomy of the knee should be considered.

The Role of Continuous Passive Motion Postoperatively

Fazalare and colleagues[13] evaluated the clinical evidence of using CPM postoperatively after treating articular cartilage lesions of the knee. Multiple medical databases were searched. No randomized controlled studies were identified. A meta-analysis could not be carried out as a result of the heterogeneity of the procedures and outcome measures. They stated that conclusions regarding the benefits of CPM postoperatively in knee cartilage surgery could not be made secondary to this heterogeneity. Also, that the clinical evidence to support the use of CPM is lacking despite the common clinical practice of CPM implementation postoperatively in knee cartilage restoration procedures.

Magnetic Resonance Imaging in the Assessment of Cartilage Repair

Domayer and colleagues[14] reviewed the clinical aspects of MF, MO, and ACI and reported the recent technical advances that have improved MRI of cartilage. They recommended morphological evaluation methods for each of the respective techniques. Finally, they provided an overview of T2 mapping and delayed gadolinium-enhanced MRI of cartilage in cartilage repair. The introduction of high-field MRI to clinical routine makes high resolution and three-dimensional imaging readily available.

Cost-Effectiveness of Different Treatments

Clar and colleagues[11] reported the current cost-effectiveness evidence on ACI. Economic models, using some assumptions about long-term outcomes that seem reasonable, suggested that ACI would be cost-effective because it is more likely to produce hyaline cartilage, which is more likely to be durable and to prevent osteoarthritis in the longer term. However, they concluded that there is insufficient evidence at present to say that ACI is cost-effective compared with MF or MO.

Discussion

This review has tried to address the following questions: 1) Is there a difference between ACI, MO, and MF regarding their results; 2) review the results of no treatment, compared with the treatment group (ie, what is the natural history of untreated small articular cartilage lesions); 3) What is the role of CPM after the surgical treatment of cartilage defects (ie, postoperatively); 4) What is the role of MRI in the assessment of cartilage defects; and 5) Is ACI cost-effective, compared with MF and MO.

In regard to the results of ACI, MF, and MO in patients with full thickness articular cartilage defects of the knee, this review has shown that there is insufficient evidence to reach conclusions on the use of ACI for treating full thickness articular cartilage defects in the knee.[10]

Although the natural history of articular cartilage lesions has not been clearly studied, significant injuries are believed to progress, resulting in degenerative arthritis of the joint.[8] Changes have been made in surgical techniques in an attempt to better manage these lesions. However, there is limited evidence that any surgical intervention significantly alters the natural history of these lesions. Randomized trials have been done to examine the outcomes of common restoration procedures performed, such as MF, MO, and ACI. Because the natural history of articular cartilage lesions has not been defined, we can assess the utility of surgical interventions only by comparing methods.

The clinical evidence to support the use of CPM is lacking despite an overwhelming abundance of basic science support and the common clinical practice of CPM implementation postoperatively in knee cartilage restoration procedures.[13] Thus, the role of CPM after surgery is still unknown.

New quantitative MRI techniques that directly visualize the molecular structure of cartilage may further advance our understanding of cartilage repair.[14] The clinical evaluation of cartilage repair tissue is a complex issue, and MRIs are becoming increasingly important both in research and in clinical routine. Finally, there is insufficient evidence, at present, to say that ACI is cost-effective compared with MF or MO.[11]

In conclusion, the natural history of cartilage lesions remains so far unknown. There is, at present, no evidence of significant difference between ACI and MF and MO. Therefore, further good quality randomized controlled trials with long-term functional outcomes are required. However, based on the data reviewed, the results may be similar and it is possible that none of the treatment methods that purport to "restore" articular cartilage are effective.

Author's Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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