Current Treatments of Isolated Articular Cartilage Lesions of the Knee Achieve Similar Outcomes

Hong-Chul Lim MD, PhD, Ji-Hoon Bae MD,
Sang-Heon Song MD, Young-Eun Park MD,
Seung-Ju Kim MD

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Abstract

Background Many surgical techniques, including microfracture, periosteal and perichondral grafts, chondrocyte transplantation, and osteochondral grafts, have been studied in an attempt to restore damaged articular cartilage. However, there is no consensus regarding the best method to repair isolated articular cartilage defects of the knee.

Questions/purposes We compared postoperative functional outcomes, followup MRI appearance, and arthroscopic examination after microfracture (MF), osteochondral autograft transplantation (OAT), or autologous chondrocyte implantation (ACI).

Methods We prospectively investigated 30 knees with MF, 22 with OAT, and 18 with ACI. Minimum followup was 3 years (mean, 5 years; range, 3–10 years). We included only patients with isolated cartilage defects and without other knee injuries. The three procedures were compared in terms of function using the Lysholm knee evaluation scale, Tegner activity scale, and Hospital for

Special Surgery (HSS) score; modified Outerbridge cartilage grades using MRI; and International Cartilage Repair Society (ICRS) repair grade using arthroscopy.

Results All three procedures showed improvement in functional scores. There were no differences in functional scores and postoperative MRI grades among the groups. Arthroscopy at 1 year showed excellent or good results in 80% after MF, 82% after OAT, and 80% after ACI. Our study did not show a clear benefit of either ACI or OAT over MF.

Conclusions Owing to a lack of superiority of any one treatment, we believe MF is a reasonable option as a first-line therapy given its ease and affordability relative to ACI or OAT. **Level of Evidence** Level II, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

The introduction of arthroscopy to knee surgery allowed for detailed study of articular cartilage disorders and initiated rapid development of diagnostic and therapeutic methods. Although several studies concerning knee cartilage lesions have been performed [4, 9, 17], the treatment of isolated lesions remains a controversial challenge.

MF, OAT, and ACI have been described for repair of symptomatic defects of the articular cartilage in the knee. Knutsen et al. [14] reported they did not find any difference in macroscopic or histologic results between ACI and MF. Bentley et al. [3] found ACI provided better results than OAT. In contrast, Horas et al. [12] reported better clinical and histologic results with OAT.

However, most cartilage lesions are associated with more extensive joint injuries, contributing to the risk for

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H.-C. Lim, J.-H. Bae, S.-H. Song, Y.-E. Park, S.-J. Kim (✉)
Korea University Medical Center, Guro Hospital, 80 Guro-dong,
Guro-gu, Seoul 152-703, South Korea
e-mail: sju627@hotmail.com

osteoarthritis. For this reason, results of current cartilage repair techniques of the isolated lesions have not been clearly evaluated and there are, to our knowledge, no comparative studies of the three procedures by one surgeon. In this study we aimed to compare the effectiveness of three different articular cartilage surgery techniques (MF, OAT, ACI) in the repair of isolated articular cartilage lesions of the knee regarding their ability to improve clinical function as assessed by functional outcome scores, postoperative radiographic assessment of cartilage repair using the Outerbridge classification, and postoperative arthroscopic assessment using the ICRS grade for repair.

Patients and Methods

We randomly divided 109 patients (120 knees) with a single symptomatic articular cartilage lesion to receive MF, OAT, or ACI from 2000 to 2008. The patients were derived from those who lived in Seoul, Korea or who were referred to our institution through another hospital. These patients were counseled regarding the surgical process and its complications and only those willing were prepared for surgery. Twenty-nine patients were excluded: four who were lost to followup, 23 who did not have adequate serial functional scores at 1, 6, 12, 24, and 36 months postoperatively, and two patients who died. Eleven patients who had undergone a secondary arthroscopic procedure on the same knee owing to trauma or other diseases such as ligament injuries, meniscal tears, and intraarticular infections also were excluded because these could affect the postoperative clinical scores even though they are not related to the cartilage procedure. None of their data were included. Therefore, the final study enrollment included 69 patients (70 knees) with focal cartilage defects of the medial and lateral femoral condyle with a stable knee and without any concomitant disease. MF was performed in 30 knees, OAT

in 22, and ACI in 18. Despite the differences in indications between the three procedures, they shared the same indications in selected cases of cartilage lesions: (1) symptomatic isolated cartilage defects (no associated knee injuries); (2) Grades 3 and 4 lesions (according to modified Outerbridge grades [20]); (3) articular cartilage defects of the medial or lateral femoral condyle; and (4) defects between 1 cm² and 4 cm² in area. In four patients who were familiar with and willing to choose the procedures, the treatment selected was dependent on the patient's choice after they were counseled regarding the surgical process and its complications. These patients were excluded from the beginning of the study owing to the potential for bias. There were 40 men and 29 women with a mean age of 28.5 years (range, 18–42 years) at the time of surgery enrolled in the study. The minimum followup was 3 years (mean, 5.7 years; range, 3–10.5 years), and the mean size of the defect was 2.74 cm² (range, 1–4 cm²). The lesions were located on the medial femoral condyle in 55 knees (79%) and on the lateral femoral condyle in 15 knees (21%) (Table 1).

For all enrolled patients, lateral and skyline radiographs of the knee and AP radiographs of both knees were taken with the patient in a weightbearing position, before surgery. All patients also underwent MRI before surgery.

All patients signed informed consent forms concerning the operative technique to be performed. The institutional review board approved the study protocol. The allocation sequence was generated by the professional statistician of our institution. The types of surgery the patients received were kept in sealed envelopes and concealed until procedures were assigned. The patients and the persons who assessed the outcomes were completely blinded to group assignment. Patient rights are protected by a law that requires patients to be informed at the time of examination about the possibility that their medical records and radiographs will be reviewed for scientific purposes.

Table 1. Preoperative demographic data for the three groups

Parameter	MF group (30 knees)	OAT group (22 knees)	ACI group (18 knees)	p value
Mean age in years (range)	32.9 (22–42)	30.4 (20–39)	25.1 (18–32)	0.232
Mean followup in years (range)	6.7 (3.5–10.5)	5.8 (3.2–7.5)	5.2 (3.0–7.2)	0.225
Gender				0.432
Male	17	12	10	
Female	12	10	8	
Lesions				0.352
Medial	23	19	13	
Lateral	7	3	5	
Mean defect size (range)	2.77 cm ² (1.2 cm ² –3.6 cm ²)	2.75 cm ² (1.0 cm ² –4.0 cm ²)	2.84 cm ² (1.5 cm ² –3.8 cm ²)	0.578
Range of motion	–3.5°–118.4°	–5.5°–119.2°	–2°–118.2°	0.335

MF = microfracture; OAT = osteochondral autograft transplantation; ACI = autologous chondrocyte implantation.

All three procedures in our study were performed by the senior author (HCL). MF was performed using specialized tapered awls. After an arthroscopic examination of the joint, in case of focal articular cartilage defect, cartilaginous remnants on the subchondral bone were débrided fully with an arthroscopic curette and shaver. Conical holes of 0.5 mm to 1 mm in diameter and 4 mm deep were punched throughout the defect at a distance of 3 mm to 4 mm apart with awls. Holes were created in the defective lesion by using instruments from appropriate angles. Creation of the holes was started from the periphery to the center of the lesion at the demarcation line of the intact cartilage.

OAT was performed after arthroscopic examination. After débridement of the fibrillated cartilage, the size of the lesion was measured using a 5-mm graduated probe and size tamp. To prepare the recipient site, the recipient tube harvester was placed over the defect. The harvesting device was perpendicular to the articular surface at the time of graft harvest. The grafts were inserted congruently so that they were not proud or recessed and they were supported at the base of the bone tunnels. We used plugs of 4, 6, and 8 mm in diameter. Each donor transplant was harvested with a larger (0.1-mm) cylinder, and the lesion was carved out with a smaller cylinder so that a press-fit transplantation of the osteochondral cylinder could be achieved. All plugs were placed at the same level with the healthy cartilage. At the end of the procedure, we moved the joint through full ROM to check that the osteochondral plugs were stable.

ACI was performed in two stages. The first stage required arthroscopy and harvesting of a 1-cm × 1-cm fragment from the margin of the trochlea. The fragment underwent enzymic digestion to release cells, and culture of the cells was performed in serum taken from the patient's blood at the time of surgery. Postoperative treatment was routine for the arthroscopy. We undertook the second stage, the arthrotomy, 6 weeks later. A periosteal flap, harvested from the tibia, was placed over the cartilage defect, fixed with sutures, and sealed with fibrin glue after which a solution of expanded chondrocytes was injected underneath the flap. After the final suture and seating with glue, the wound was carefully closed in layers with non-absorbable sutures.

The rehabilitation program was identical after all three operative techniques. The patients were told to perform certain rehabilitative exercises using a continuous passive motion device 2 to 4 hours per day for 6 to 8 weeks. The patients were allowed to bear weight partially on their tiptoes for 6 to 8 weeks. After 8 weeks, full weightbearing was permitted and the patient returned to work. Normal activities of daily living were resumed 4 to 6 months after treatment.

For clinical assessment, we used three validated questionnaires: the (1) Lysholm knee evaluation scale [16],

(2) Tegner activity scale [28], and (3) HSS knee scores [13]. We performed assessments preoperatively; at 1, 6, 12, 24, and 36 months postoperatively; and at the last followup.

Second MRI studies were performed 12 to 14 months postoperatively on 61 knees. Three of us (SJK, HCL, JHB) independently classified and scored the MRI findings using the modified classification system of Outerbridge [20, 23, 27].

A second arthroscopy was performed in 52 knees 12 to 18 months after the procedure. A probe was used to assess the consistency of the graft. The repair was observed and assessed using the ICRS grading system [29].

The differences in the mean outcome scores between preoperatively and postoperatively were analyzed using the two-tailed test. Statistical comparison of functional scores, Outerbridge grades, and ICRS grades among the groups was analyzed using the Kruskal-Wallis test for nonparametric data. A *p* value less than 0.05 was taken to be significant. The data were recorded using Microsoft[®] Excel[®] 2007 version (Microsoft Corp, Redmond, WA, USA) and analyzed using SPSS[®] software (SPSS Inc, Chicago, IL, USA). A power analysis was performed using the arthroscopic grades as the primary variables and data from a surgical population at our institution that were representative of the study population. This analysis indicated that a sample size of at least 14 patients per group was necessary for a between-group difference of the arthroscopic grades with an alpha of 0.05 and power of 80%. For the MRI classification, an alpha 0.05 and power of 86% were indicated. Radiographic parameters were tested for concurrence and reproducibility by intraobserver and interobserver studies using Pearson correlation coefficients. The arthroscopic grades were tested by interobserver studies. Intraobserver studies were not performed. The correlations for intraobserver measures of MRI classification were 0.912, 0.904, and 0.898; the mean Pearson correlation coefficient was 0.912. The correlation coefficients for interobserver measures ranged from 0.887 to 0.981. Regarding arthroscopic grades, the correlation coefficient was between 0.758 and 0.966.

Results

After surgery, all three procedures showed improvement in functional outcome scores. There were no differences in the results when using the three scoring systems (Table 2) (Fig. 1). The mean postoperative ROM was 115.1° (111.5° – 119.5°) at the final followup and there was no difference in postoperative ROM among the groups.

Postoperative MRI showed Outerbridge Grades 1 or 2 in 20 of 25 knees (80%) after MF (Fig. 2), 17 of 20 knees (85%) after OAT (Fig. 3), and 13 of 16 knees (81%) after ACI (*p* = 0.483) (Table 3).

Table 2. Overall clinical scores at 5 years postoperative

Procedures (number of knees)	Lysholm scale (mean $\pm$ SD)			Tegner scale (mean $\pm$ SD)			HSS scores (mean $\pm$ SD)		
	Preoperative	Postoperative	p value	Preoperative	Postoperative	p value	Preoperative	Postoperative	p value
MF (25)	51.2 $\pm$ 6.2	85.6 $\pm$ 6.8	$p < 0.001$	2.8 $\pm$ 1.4	5.1 $\pm$ 1.5	$p < 0.001$	78.22 $\pm$ 9.12	87.60 $\pm$ 4.56	$p < 0.001$
OAT (22)	53.2 $\pm$ 7.2	84.8 $\pm$ 5.5	$p < 0.001$	2.7 $\pm$ 1.5	5.3 $\pm$ 1.2	$p < 0.001$	78.66 $\pm$ 7.23	88.12 $\pm$ 4.15	$p < 0.001$
ACI (18)	52.4 $\pm$ 6.4	84.6 $\pm$ 6.1	$p < 0.001$	2.9 $\pm$ 1.8	5.2 $\pm$ 1.3	$p < 0.001$	77.52 $\pm$ 8.16	87.51 $\pm$ 4.58	$p < 0.001$
p value		0.432			0.213			0.516	

MF = microfracture; OAT = osteochondral autograft transplantation; ACI = autologous chondrocyte implantation; HSS = Hospital for Special Surgery.

Fig. 1 The overall Lysholm, Tegner, and HSS clinical scores at postoperative 5 years are shown. MF = microfracture; OAT = osteochondral autograft transplantation; ACI = autologous chondrocyte implantation; HSS = Hospital for Special Surgery; * $p > 0.05$.

Of the 52 cartilage defects, 43 (82%) had completely filled with tissue resembling cartilage. Arthroscopy at 1 year revealed ICRS Grades 1 or 2 in 16 of 20 patients (80%) after MF, 14 of 17 patients (82%) after OAT, and 12 of 15 patients (80%) after ACI (Fig. 4) ($p = 0.686$) (Table 4).

Three reoperations were performed in the MF group, one in the OAT group, and two in the ACI group. In the MF group, two patients underwent reoperations owing to recurrent knee pain during sports activity. One patient was slow to mobilize and required arthroscopy and arthrolysis. In the OAT group, the activities of one patient were limited because of knee problems. A secondary arthroscopy was performed on this patient and revealed that one osteochondral plug was prominent in the surrounding cartilage causing abrasion of the opposite tibial cartilage. In the ACI group, one patient had recurrent knee pain and one had persistent articular effusion which required arthroscopic examinations.

Discussion

The goals of cartilage defect repair should be a combination of symptom relief and prevention of early joint degeneration. Traditional resurfacing techniques, such as drilling and MF, have proven to be safe and effective for treating articular cartilage defects of the knee, but they do not restore normal hyaline cartilage and have only a short-term success rate [2, 6]. In this study we aimed to compare the effectiveness of three different articular cartilage surgery techniques (MF, OAT, ACI) for repair of isolated articular cartilage lesions of the knee regarding their ability to improve clinical function as evaluated by functional scores and postoperative radiographic and arthroscopic assessment.

Our study has some limitations. First, the study involves a relatively small number of patients. A power analysis was performed suggesting sufficient numbers but a larger study population may have led to conflicting results. Our study might be underpowered for a meaningful statistical analysis because we excluded patients who had cartilage defects with other concomitant knee injuries. However, we believe that our data and results are provocative and should be read by specialists in this field. Second, the followup rate was relatively low owing to strict serial postoperative evaluations. Third, only the clinical scores were reviewed at the medium term. Second MRI and second-look arthroscopy were evaluated at approximately 1 year postoperatively.

OAT has some advantages over MF when used with young athletes [8]. It was reported that there were better results and fewer failures with the OAT procedure and more athletes were able to return to their preinjury level of sports participation after having the OAT procedure compared with the MF procedure [8]. Previously, Gudas et al. [7] reported that patients treated with MF showed deterioration of clinical scores with time in comparison to patients treated with OAT. However, they investigated the results of children younger than 18 years with osteochondritis dissecans only. The mean age of the patients in our study was 28.5 years. Furthermore, OAT is a technically

Fig. 2A–B (A) A preoperative MR image shows collapse of the weightbearing surface of the medial femoral condyle in a 51-year-old woman with a cartilage defect of the right knee. (B) Twelve months after the MF procedure, the articular contour of the medial femoral condyle is restored.

Fig. 3A–B (A) This preoperative MR image shows collapse of the weightbearing surface of the lateral femoral condyle in an 18-year-old woman with a cartilage defect of the right knee. (B) One year after OAT of the lateral femoral condyle, the articular contour is congruent, but a subchondral cyst is seen.

Table 3. Overall MRI results at 1 year postoperative

Outerbridge grades	Microfracture Number (%)	Osteochondral autograft transplantation Number (%)	autologous chondrocyte implantation Number (%)
1	4 (16%)	4 (20%)	3 (19%)
2	16 (64%)	13 (65%)	10 (62%)
3	3 (12%)	3 (15%)	2 (13%)
4	2 (8%)	0 (0%)	1 (6%)
Total	25 (100%)	20 (100%)	16 (100%)

demanding procedure and the donor site location and size of the osteochondral grafts are important for long-term articular cartilage survival. Drawbacks of this technique are limited availability of donor tissue and donor site morbidity [11]. The number of plugs that can be used is limited. Although the osteochondral plugs are taken from a relatively nonweightbearing area of the joint, donor site morbidity has been reported in approximately 3% of patients [10]. At the recipient site, the mechanical stability and positioning of the grafts are also critical. Proud and recessed plugs have worse outcomes than flush plugs, most

likely secondary to abnormal mechanical stress [5]. In our series, the activities of one patient were compromised because of a prominent plug and revision was required replacing the prominent osteochondral plug. OAT also may create symptoms owing to an incongruent bone-bone interface because relatively flat, thin articular cartilage is used to replace round, thick cartilage.

For ACI, no relationship between defect size and clinical outcome has been found, which implies ACI can be used for cartilage defects of all sizes [15]. It has been recommended for defects from 2 cm² to 12 cm². However, ACI is a two-step procedure and is troublesome for patients. The second procedure may occur from 6 weeks to several months after the biopsy and also may lead to complications. Clinical failures after ACI have been reported in 6% to 13% of patients [18, 19, 22]. Failure of the ACI may occur from poor bone integration, poor repair-tissue quality (soft graft), graft detachment (delamination), or degeneration of the repair tissue [19]. When the delamination is displaced, the ACI site is empty and the displaced repair tissue often is found as an intraarticular loose body elsewhere in the joint [1]. Degeneration of the ACI tissue most often presents as pain years after surgery. An increased inflammatory

Fig. 4A–B (A) A preoperative arthroscopic image shows a Grade 4 cartilage defect. (B) Thirteen months after our patient, a 22-year-old man, underwent ACI of the lateral femoral condyle, a Grade 2 articular cartilage lesion with good coverage can be seen.

Table 4. Overall arthroscopic results at 1 year postoperative

ICRS grades	Microfracture Number (%)	Osteochondral autograft transplantation Number (%)	Autologous chondrocyte implantation Number (%)
1 = excellent	2 (10%)	3 (18%)	3 (20%)
2 = good	14 (70%)	11 (64%)	10 (66%)
3 = fair	2 (10%)	2 (12%)	1 (7%)
4 = poor	2 (10%)	1 (6%)	1 (7%)
Total	20 (100%)	17 (100%)	15 (100%)

ICRS = International Cartilage Repair Society.

response and negative influences on joint proprioception after two procedures performed shortly after each other could increase the risk for early osteoarthritis. In our study, one patient had recurrent knee pain and one had persistent articular effusion which required arthroscopic examinations after ACI. The formation of intraarticular adhesions causing knee stiffness is the most common arthrotomy-related complication, occurring in approximately 5% of patients treated with ACI [19]. Periosteal complications include fibrous overgrowth of the periosteal cover (periosteal

hypertrophy) and separation and detachment of a hypertrophic periosteal cover from the underlying hyaline repair (periosteal delamination). Periosteal hypertrophy is commonly seen on histologic examination and arthroscopy and may be symptomatic in as much as 20% of patients [19]. An additional limitation of ACI and its derivatives is that chondrocytes tend to dedifferentiate during monolayer expansion, which decreases their extracellular cartilage matrix formation potential [21]. The superficial layer is a tissue of varying morphologic features [25] and does not have the same mechanical properties as those of native hyaline-like cartilage.

In contrast, the MF technique was popularized by Steadman et al. [26] and often is considered to be the first-line treatment option for full-thickness articular cartilage defects because of its minimally invasive nature, technical ease, limited surgical morbidity, and low cost. The lesion is débrided to stable, squared-off edges with minimal instrumentation. Also, MF has been advocated over drilling because less heat and necrosis are thought to occur. Failure and complications of MF are shown as poor fill of repair tissue and chondral fissures. In the first few months after MF, MRI shows repair tissue of intermediate signal intensity that typically is thinner than the adjacent native articular cartilage [1]. However, Recht et al. [24] reported that with time, the amount of repair tissue increases, with the optimal result being 100% defect fill with a congruent articular surface and repair tissue of signal intensity similar to that of native articular cartilage. Fibrocartilage repair tissue may not be sufficient for weightbearing surfaces of the knee for physically active athletes and more durable repair tissue may be needed. However, our results showed that postoperative functional outcome scores improved after the MF, OAT, and ACI procedures and there were no differences in the results when using the three scoring systems. Also, postoperative MRI grades and arthroscopic results were similar among the groups.

Our study showed all three procedures give encouraging clinical results but did not show a clear outcome benefit for either ACI or OAT over MF at an average followup of 5 years. We believe that when considering pain, function, and overall failure rates with time, MF seems to be a reasonable option for treating articular cartilage defects at intermediate-term followup. Properly powered and long-term followup studies are needed to determine how durable this type of repair really is. These studies will provide pilot data to justify our study.

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