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ORIGINAL ARTICLE

Treatment of Focal Articular Cartilage Defects in the Knee

A Systematic Review

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Abstract We asked whether autologous chondrocyte implantation or osteochondral autograft transfer yields better clinical outcomes compared with one another or with traditional abrasive techniques for treatment of isolated articular cartilage defects and whether lesion size influences this clinical outcome. We performed a literature search and identified five randomized, controlled trials and one prospective comparative trial evaluating these treatment techniques in 421 patients. The operative procedures included autologous chondrocyte implantation, osteochondral autograft transfer, matrix-induced autologous chondrocyte implantation, and microfracture. Minimum followup was 1 year (mean, 1.7 years; range, 1–3 years). All studies documented greater than 95% followup for clinical outcome measures. No technique consistently had superior results compared with the others. Outcomes for microfracture tended to be worse in larger lesions. All studies reported improvement in clinical outcome measures in all treatment groups when compared with preoperative assessment; however, no control (nonoperative) groups were used in any of the studies. A large prospective trial investigating these techniques with the addition of a control group would be the best way to definitively address the clinical questions.

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Level of Evidence: Level II, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Full-thickness articular cartilage defects have limited regenerative potential. These defects can cause knee discomfort and swelling and eventually may contribute to premature development of osteoarthritis [9]. In a report on 31,516 arthroscopies, these lesions occurred in a minimum of one of every 100 knee arthroscopies [13]. An ideal treatment for these lesions would result in regeneration of the hyaline cartilage in the area of the defect that is integrated with surrounding normal cartilage and mechanically functional.

Multiple techniques have been developed during the past several decades to address this difficult problem. Subchondral drilling [38], abrasion [28], and microfracture [44] have been reported as methods for stimulation of articular cartilage healing. These methods all involve breaching the subchondral bone to allow pluripotent stem cells from the marrow to remodel the fibrin clot in the defect into fibrocartilage. More recently, methods not so dependent on recruitment of pluripotent cells have been proposed. Osteochondral autograft transfer (OAT) has been developed to replace articular cartilage defects with osteochondral autografts [3, 22]. This technique involves harvesting one large graft or multiple smaller cylinders (mosaicplasty) from minimal weightbearing portions of the distal femur and transplanting them to cover defects in higher weightbearing areas. Autologous chondrocyte implantation (ACI) involves placement of cultured chondrocytes in the articular cartilage defect [5, 20]. The

original method relied on a sutured periosteal cover (ACI-P) to keep the chondrocytes in the desired location and porcine-derived collagen covers (ACI-C) were developed later. More recently, suture-free biodegradable scaffolds have been used in matrix-induced autologous chondrocyte implantation (MACI) [10].

The surgeon considering treatments of these articular defects thus is faced with multiple options. Review of the literature yields numerous retrospective case series of results of abrasive techniques [28, 38, 42–44], OAT [3, 18, 21, 26], and ACI [4–7, 15, 32, 33, 36, 37, 39]. These case series are Level IV data without comparison groups, many of which are written by the originators of the surgical technique being described. A recent review by Jakobsen et al. [27] identified 61 publications on cartilage repair, varying from prospective, randomized studies to case series, and noted their generally low methodologic quality.

We therefore embarked on a systematic review of the best evidence in the literature to answer the following clinical questions: (1) does one advanced cartilage repair technique such as ACI or OAT yield better clinical outcomes than another or show superior outcomes to traditional abrasive techniques for treatment of isolated Outerbridge Stage 3 or 4 articular cartilage defects?; and (2) does lesion size influence clinical outcome to a greater extent in one technique than in others?

Materials and Methods

To address the clinical questions outlined, we elected to perform a systematic review of Levels I and II studies. We did not require use of any one specific clinical outcome measure for inclusion as substantial diversity in clinical outcome measures was anticipated. If sufficient studies comparing similar groups, interventions, and outcome measures were identified, a meta-analysis was planned. If the resulting data were too heterogeneous for meta-analysis, clinical results would be summarized and expressed in tables for review by readers.

We performed a literature search of MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, and the Cumulative Index for Nursing and Allied Health Literature (CINAHL) to identify all prospective comparative studies evaluating operative treatment of articular cartilage defects of the knee with ACI or OAT. The MEDLINE search of articles published between January 1, 1966, and January 1, 2007, yielded 11,885 papers containing any one of the follow terms: autologous chondrocyte, ACI, osteochondral, OATS, mosaicplasty, microfracture, abrasion, or chondroplasty. These studies were narrowed to 1092 by requiring that they also contain the term knee. The search then was limited to English articles on human subjects classified by MEDLINE as randomized, controlled trials, clinical trials, controlled clinical trials, or multicenter studies. We then reviewed the abstracts of the resulting 37 studies.

Publications were included in this review if they were prospective comparative studies comparing results of treatment of full-thickness (Outerbridge Grade 3 or 4) lesions. The modified Outerbridge classification was defined as follows: Grade 0, normal cartilage; Grade 1, cartilage softening and swelling; Grade 2, fissures not reaching subchondral bone; Grade 3, fissures to subchondral bone; and Grade 4, exposed subchondral bone [34, 35]. Studies were required to include at least 30 patients, have at least 1 year of followup, and compare either ACI or OAT with another treatment method. We identified and included five randomized, controlled trials [1, 2, 19, 29, 45] and one prospective comparative trial [24] in the previously cited literature review. All references in these articles were reviewed manually in search of other possible studies and none was identified.

Twenty-nine studies were excluded from the analysis because they were not related to articular cartilage repair (18 papers) or they were not trials comparing two or more repair techniques (11 studies). Two additional studies were excluded because one had too few subjects and less than 1 year of followup [14] and the other was a trial comparing two different techniques of ACI [16].

A search of the Cochrane Central Register of Controlled Trials was done using the same search strategy yielding 23 studies, including the six trials identified previously. No other studies meeting inclusion and exclusion criteria were identified. A search of EMBASE using these criteria yielded 335 studies including the six trials identified previously. The remaining studies did not meet criteria. Use of the same search on CINAHL yielded 133 studies. The three randomized, controlled trials identified already were included in the previously mentioned study and the remaining 130 did not meet criteria.

A templated evidence-based medicine literature review form was used to assist in the systematic review of articles and the data were collected [17, 30, 41]. Demographic data presented for comparison include publication date, author, journal, surgical procedures evaluated, total number of subjects, mean patient age, method of randomization, percent traumatic lesions, interval from injury to surgery, and lesion size and location (Table 1). Additional study details, including mean followup, details of followup evaluations, the presence of cointerventions, and rehabilitation protocol were noted (Table 2). Primary and secondary clinical outcomes, results of arthroscopic and histologic evaluations, and the use of independent observers also were recorded (Table 3).

Table 1. Selected demographic data from included studies

Level	Year of study	Study	Journal	Group 1	Group 2	Total enrolled participants	Mean patient age (years)	Method of randomization	Percent traumatic	Duration of symptoms (months)	Lesion size (cm^2)*	Lesion location
I	2005	Gudas et al. [19]	Arthroscopy	OAT arthroscopic	Microfracture	60	24.3	Envelope	56%	21.3	2.8 (1–4)	84% MFC 16% LFC
I	2005	Bartlett et al. [1]	JBJS Br	ACI-C	MACI (3D)	91 (112)†	33.5	Block randomization	43%	102.7	6.1 (1–22)	45% MFC 10% LFC 32% Patella 13% Trochlea
I	2004	Knutsen et al. [29]	JBJS Am	ACI-P	Microfracture	80	32.2	Envelope	65%	36	4.8 (2–10)	89% MFC 11% LFC
I	2004	Visna et al. [45]	ACB	MACI (3D)	Abrasion	50 (60)†	30.8	Envelope	86%	NR	3.72 (2–10)	55% MFC 18% LFC 18% Patella 8% Tibial plateau
I	2003	Bentley et al. [2]	JBJS Br	ACI-P: 6 ACI-C: 46	OAT open	100	31.3	Random number	46%	86.4	4.66 (1–12.2)	53% MFC 18% LFC 25% Patella 1% Tibial plateau 3% Trochlea
II	2003	Horas et al. [24]	JBJS Am	ACI-P	OAT open	40	33.4	Alternating	100%	NR	3.75 (3.2–5.6)	82% MFC 18% LFC

*Values expressed as mean, with range in parentheses; †number of lesions in parentheses; multiple lesions addressed in some knees; OAT = osteochondral autograft transplant; MFC = medial femoral condyle; LFC = lateral femoral condyle; JBJS Br = Journal of Bone and Joint Surgery–British Edition; MACI = matrix-induced autologous chondrocyte implantation; ACI-C = autologous chondrocyte implantation–collagen cover; JBJS Am = Journal of Bone and Joint Surgery–American Edition; ACI-P = autologous chondrocyte implantation–periosteal patch; ACB = Acta Chirurgica Belgica; 3D = three dimensional; NR = not reported.

Table 2. Followup

Study	Followup (years) for primary clinical outcome	Participants evaluated clinically	Participants evaluated arthroscopically	Participants evaluated histologically	Cointerventions	CPM	Time to partial weightbearing	Time to full weightbearing
Gudas et al. [19]	3	57 (95%)	34 (57%)*	25 (42%)*	None	No	4 weeks	8 weeks
Bartlett et al. [1]	1	91 (100%)	42 (46%)	25 (27%)	None	No	1 day	10 days
Knutsen et al. [29]	2	80 (100%)	77 (96%)	67 (84%)	None	Yes	1 day	8–12 weeks
Visna et al. [45]	1	50 (100%)	4 (8%)†	4 (8%)†	22 (MACI group) 19 (abrasion group)	NR	3 weeks	6–8 weeks
Bentley et al. [2]	1	100 (100%)	60 (60%)‡	19 (19%)§	NR	No	NA	1 day
Horas et al. [24]	2	40 (100%)	12 (30%)*	11 (28%)*	None	Yes	2 weeks	12 weeks

*Nonrandom selection of patients to evaluate arthroscopically and biopsy; †all from MACI group; ‡64% of patients with ACI and 55% of patients with OAT; §all from ACI groups; CPM = continuous passive motion; NR = not reported; NA = not applicable; MACI = matrix-induced autologous chondrocyte implantation; ACI = autologous chondrocyte implantation; OAT = osteochondral autograft transplant.

Details of the study design used by the authors to control major confounding variables and possible biases were recorded and evaluated on a published evidence-based medicine form [41]. Each was assigned a level of evidence according to published guidelines of the *Journal of Bone and Joint Surgery* [47] and a modified Coleman Methodology Score [11] (Table 1). The modified Coleman Methodology Score is an attempt to quantify the overall quality of study design and execution, including sample size, length of followup, blinding, adequacy of description of procedures and rehabilitation protocol, and other study characteristics [11, 12].

All six studies required the patients to have isolated Outerbridge Stage 3 or 4 lesions without generalized osteoarthritis, although two studies did include patients in whom multiple lesions were addressed [1, 45]. The majority of lesions were on the femoral condyles, although several studies included lesions in other regions of the knee [1, 2, 45]. All authors required a stable knee except for Visna et al. [45], whose patients had concurrent anterior cruciate ligament reconstruction and were included in both groups (seven of 25 patients in the MACI group and three of 25 in the abrasion group). Lesion size and duration of symptoms varied considerably among the studies but were equal between treatment groups in all six studies. All studies focused on patients between skeletal maturity and an upper age limit between 40 and 50 years. The study by Gudas et al. [19] was unique because they included only patients who were competitive or well-trained athletes by International Cartilage Repair Society criteria, whereas others included patients regardless of activity level [8]. Trauma was the most common etiology of the lesions in all studies. Gender, age, body mass index, and lesion location and etiology were equal between treatment groups in all studies reviewed.

Two studies used the microfracture technique as described by Steadman et al. [42–44] without substantial modifications [19, 29]. Arthroscopic awls were used to make multiple 2-mm holes 3 to 4 mm apart in the affected region.

Visna et al. [45] used the abrasion technique as described by Johnson [28]. Abrasion was completed to 1 to 2 mm using the arthroscopic shaver.

Osteochondral autograft transfer was performed in three studies by press-fitting osteochondral plugs from the margins of the trochlea into débrided cartilage defects. Bentley et al. [2] attempted to leave the transplanted cartilage slightly proud to ensure contact with the tibia, whereas the other groups attempted to align the grafts with the surrounding cartilage surface. Bentley et al. [2] and Gudas et al. [19] used osteochondral plugs of one fixed diameter, whereas Horas et al. [24] used multiple sizes. Gudas et al. [19] included only all-arthroscopic procedures, whereas Bentley et al. [2] and Horas et al. [24] performed the procedure through a medial or lateral arthrotomy.

Autologous chondrocyte implantation was performed in four studies using relatively similar methods (Table 4) [1, 2, 24, 29]. Matrix-induced autologous chondrocyte implantation was performed in two studies [1, 45]. Both groups used Tissucol® (Baxter AG, Vienna, Austria) as the matrix and implanted between five and 10 million cells 3 to 5 weeks after harvest.

Among the six studies, the minimum followup was 1 year (mean, 1.7 years; range, 1–3 years). All had greater than 95% followup for clinical outcome measures, whereas only Knutsen et al. [29] were able to obtain greater than 80% followup for arthroscopic and histologic evaluations. Rehabilitation protocols generally were similar, although time to partial and full weightbearing varied among studies (Table 2). All authors used identical rehabilitation protocols of both treatment groups in their studies.

Multiple clinical scoring systems were used to quantify clinical outcomes. International Cartilage Repair Society cartilage repair assessment scores were used to quantify

Table 3. Clinical, arthroscopic, and histologic data

Study	Primary clinical outcome*	Secondary clinical outcome*	Arthroscopic findings†	Histologic findings	Independent observer	Additional findings
Gudas et al. [19]	HSS ($p < 0.01$) OAT = 91.1 ± 4.1 MFx = 80.6 ± 4.6	ICRS ($p < 0.001$) OAT = 89 ± 4 MFx = 75 ± 4 Percent return to sport OAT = 93% MFx = 52%	Percent with CRA 8–12 ($p = 0.004$) OAT = 79% MFx = 45%	OAT: 100% hyaline cartilage MFx: 57% fibrocartilage 43% fibroelastic tissue	Yes	Patients younger than 30 years had better HSS score in both groups ($p = 0.008$) Patients with a traumatic defect had better HSS scores that those with osteochondritis dessicans in both groups ($p = 0.004$) Lesions > 2 cm^2 in central medial femoral condyle had lower HSS scores in MFx group ($p < 0.05$) but no significant difference in OAT group
Bartlett et al. [1]	Improvement in Mod Cinn ($p = 0.32$) MACI = 19.6 ACI-C†† = 17.5	VAS (NS) MACI = 4.1 ACI-C = 4.3 Stanmore (NS) MACI = 2.1 ACI-C = 2.2	Percent with CRA 8–12 ($p = 0.3$) MACI = 66.6% ACI-C = 79.2%	Percent with hyalinelike or mixed hyaline/fibrocartilagelike (NS) MACI = 36.4% ACI-C = 42.9%	No	Patients younger than 35 years had better clinical outcome ($p = 0.03$)
Knutsen et al. [29]	SF-36 PC ($p = 0.01$) MFx = 46 ± 2 ACI-P = 42 ± 2	Lysholm (NS) MFx = 75 ± 4 ACI-P = 71 ± 5 VAS (NS) MFx = 31 ± 4 ACI-P = 35 ± 5	CRA ($p = 0.17$) MFx = 9.1 ACI-P = 8.1	Percent with hyalinelike or mixed hyaline/fibrocartilagelike ($p = 0.08$) MFx = 29% ACI-P = 50%	Yes	Patients younger than 30 years ($p = 0.007$) and patients with Tegner scores > 4 ($p = 0.0005$) had better SF-36 scores in both groups Higher SF-36 scores in MFx group associated with lesion < 4 cm^2 ($p = 0.003$)
Visna et al. [45]	Lysholm ($p = 0.001$) MACI = 86 ± 9 Abrasion = 74 ± 11	IKDC ($p < 0.05$) MACI = 76 ± 13 Abrasion = 68 ± 10 Tegner ($p < 0.01$) MACI = 5.9 ± 0.8 Abrasion = 4.2 ± 1.1	CRA MACI = 8.5 Abrasion = NR	Histology on four samples revealed evidence of hyaline-like cartilage; fibroblastlike cells (in two)	No	

Table 3. continued

Study	Primary clinical outcome*	Secondary clinical outcome*	Arthroscopic findings†	Histologic findings	Independent observer	Additional findings
Bentley et al. [2]	Mod Cinn > 55 ($p = 0.27$) ACI = 88% OAT = 69%	Medial femoral condyle lesions ONLY Mod Cinn > 55 ($p = 0.03$) ACI = 88% OAT = 74%	Percent with CRA 8–12 ($p < 0.01$) ACI = 82% OAT = 34%	Percent with hyalinelike or mixed hyaline/fibrocartilagelike ACI = 74% OAT = NR	No	Seven poor results, all in OAT group Technique documented placing plugs slightly prominently
Horas et al. [24]	Lysholm ($p < 0.05$) OAT = 74 ± 6 ACI-P = 67 ± 8	Tegner (NS) OAT = 5 ± 1 ACI-P = 5 ± 1 Meyers (NS) OAT = 17 ± 2 ACI-P = 16 ± 3	No objective data	OAT patients with hyaline cartilage not integrated into surrounding cartilage; ACI-P specimens with mainly fibrocartilage, focalized areas of hyalinelike cartilage deep	No	

*Values expressed as mean ± standard deviation when available; clinical outcome measures used: HSS = Hospital for Special Surgery clinical score (higher score indicates increased function); ICRS = International Cartilage Repair Society clinical score (higher score indicates increased function); Mod Cinn = Modified Cincinnati score (higher score indicates increased function); VAS = visual analog scale (higher score indicates increased pain); Stanmore score (lower score indicates increased function); SF-36 PC = SF-36 Physical Component score (higher score indicates increased function); Lysholm score (higher score indicates increased function); IKDC = International Knee Documentation Committee subjective score (higher score indicates increased function); Tegner activity score (higher score indicates increased level of activity); Meyers rating scale (higher score indicates increased function); †CRA = International Cartilage Repair Society cartilage repair assessment (higher score indicates more normal cartilage; 12 = normal cartilage); OAT = osteochondral autograft transplantation; MFx = microfracture; MACI = matrix-induced autologous chondrocyte implantation; ACI-C = autologous chondrocyte implantation–collagen cover; ACI-P = autologous chondrocyte implantation–periosteal cover; NS = not statistically significant; NR = not reported.

Table 4. Autologous chondrocyte implantation technique

Study	Donor site	Culture laboratory	Incubation time (weeks)	Number of cells implanted	Cover	Method of cover attachment
Bartlett et al. [1]	Trochlear margins	Verigen (Leverkusen, Germany)	3–5	NR	Collagen	Suture and fibrin glue
Knutsen et al. [29]	Proximal medial femoral condyle	Genzyme (Cambridge, MA)	4	NR	Periosteum	Suture and fibrin glue
Bentley et al. [2]	Trochlear margins	In house	3–5	5–10 $\times$ 10^6	Collagen/periosteum	Suture and fibrin glue
Horas et al. [24]	Proximal medial femoral condyle	In house	2–3	3–6 $\times$ 10^6	Periosteum	Suture

NR = not reported.

arthroscopic findings in five of the six studies. Four studies attempted to quantify the percentage of hyaline cartilage seen histologically (Table 3).

Selection bias in each study was influenced by patient inclusion criteria and method of randomization to groups. All studies had clear inclusion criteria that were similar and all but Horas et al. [24] used a random method of patient allocation. However, in four studies, there was selection bias in choosing which patients underwent arthroscopic and histologic evaluation that was influenced by factors including patient consent or the occurrence of a subsequent injury, or a choice was made to focus these evaluations on one treatment group only or specific patients in each group.

Performance bias was carefully limited in all studies. Lesion size and location, patient age, and rehabilitation protocol were similar between treatment groups in each study.

Only the study by Visna et al. [45] included patients who underwent cointerventions at the same time as the index procedure and these patients were distributed equally between the two groups.

Transfer bias was minimized in all studies regarding clinical followup, with each group attaining at least 95% followup. However, only Knutsen et al. [29] attained greater than 80% followup for the arthroscopic and histologic evaluations. Accepted followup has been defined as 70% of the study population, although greater than 80% of the study population is preferred [17, 46, 47].

Detection bias was minimized by Gudas et al. [19] and Knutsen et al. [29] by using independent observers to evaluate outcomes; however, the other four studies do not have this independent observation. Validated patient-oriented outcome measures such as the SF-36 [46] or the International Knee Documentation Committee [23] rating scale were not used by Bartlett et al. [1], Bentley et al. [2], and Horas et al. [24].

As described, all six studies included in this review were subject to some degree of bias. The modified Coleman Methodology Score [11] is an attempt to quantify the degree to which possible bias is controlled. The highest score (least bias) was noted in the study by Knutsen et al. [29]. The nonrandomized study by Horas et al. [24] yielded the lowest score (Table 1).

Results

Comparing OAT with microfracture, Gudas et al. [19] reported the OAT group had better ($p < 0.01$) clinical scores, more normal-appearing ($p = 0.004$) cartilage on visual assessment, and a subjectively greater percentage of hyaline cartilage histologically. Bartlett et al. [1] found no clinical, arthroscopic, or histologic differences between MACI and ACI-C. In comparing microfracture with ACI-P, Knutsen et al. [29] noted better ($p < 0.01$) SF-36 scores in the microfracture group but no difference in other clinical measures or arthroscopic or histologic analyses. Visna et al. [45] compared MACI with abrasion and reported improved ($p < 0.001$) clinical scores with MACI. Bentley et al. [2] and Horas et al. [24] compared OAT with ACI. Bentley et al. [2] noted more normal ($p < 0.01$) cartilage on arthroscopic examination in the ACI group, whereas Horas et al. [24] reported an improved ($p < 0.05$) clinical score with OAT.

Three of the six studies reviewed included analysis of influence of lesion size on outcome [1, 19, 29]. Gudas et al. [19] reported clinical outcomes of microfracture were worse in lesions larger than 2 cm^2 ($p < 0.05$). They observed no association between clinical outcomes and lesion size when patients were treated with OAT. Knutsen et al. [29], however, reported worse clinical outcomes in lesions greater than 4 cm^2 when treated with microfracture ($p < 0.003$) but noted no association between clinical outcome and size after ACI. Bartlett et al. [1] reported no dependence of clinical outcome on lesion size for lesions treated with ACI or MACI.

The five studies that reported preoperative clinical scores found improvement in clinical outcome measures in all treatment groups at the end of the study when compared with preoperatively (Table 3). Combining the patients in

Table 5. Complications

Study	Treatment group	Number of patients	Arthrofibrosis	Superficial wound infection	Tissue hypertrophy	Reactive synovitis	Deep venous thrombosis	Postoperative hemarthrosis	Proud osteochondral graft
Gudas et al. [19]	OAT	28		2 (7.1%)					1 (3.6%)
	Microfracture	29	1 (3.4%)						
Bartlett et al. [1]	ACI-C	44	3 (6.8%)		4 (9.1%)				
	MACI	47	3 (6.4%)	1 (2.1%)	3 (6.4%)				
Knutsen et al. [29]	ACI-P	40			10 (25%)				
	Microfracture	40	1 (2.5%)		3 (7.5%)				
Visna et al. [45]	MACI	25				6 (24%)			
	Abrasion	25							
Bentley et al. [2]	ACI-P/C	58							
	OAT	42	3 (7.1%)	1 (2.4%)			1 (2.4%)		
Horas et al. [24]	ACI-P	20	3 (15%)						
	OAT	20	3 (15%)	1 (5%)				2 (10%)	

OAT = osteochondral allograft transfer; ACI-C = autologous chondrocyte implantation–collagen cover; MACI = matrix-induced autologous chondrocyte implantation; ACI-P = autologous chondrocyte implantation–periosteal cover.

both treatment arms, Gudas et al. [19] reported the Hospital for Special Surgery score improved ($p < 0.05$) from a mean of 77 preoperatively to 86 at 1 year and improvement ($p < 0.05$) in International Cartilage Repair Society score improved from 51 to 82 during the same period. Similarly, Bartlett et al. [1] reported a 19-point improvement ($p < 0.01$) in the mean Cincinnati knee score at 1 year. Knutsen et al. [29] noted an improvement ($p < 0.0001$) in visual analog pain score from 55 to 33 2 years after surgery and increases ($p = 0.003$) in Lysholm knee score from 56 to 73 and SF-36 physical component scores from 39 to 44. Visna et al. [45] described an improvement in Lysholm score from 50 to 80, increase in International Knee Documentation Committee score from 43 to 72, and improvement in Tegner activity score from 2.7 to 5.1 ($p < 0.01$). Horas et al. [24] noted increases in Lysholm score from 27 to 70 over 2 years, improvement in Meyers score from 8 to 17, and increase in Tegner activity score from 2 to 5 during the same period. Bentley et al. [2] did not provide preoperative clinical scores.

All six studies reported complications (Table 5). Common complications encountered in the reviewed papers included arthrofibrosis, superficial wound infections, and tissue hypertrophy. Much lower incidences of deep venous thrombosis, hemarthrosis, and graft malpositioning were reported. Arthrofibrosis appeared with equal frequency in all treatment groups. Superficial wound infection, deep venous thrombosis, and hemarthrosis appeared most commonly with OAT. Tissue hypertrophy surrounding the lesion and reactive synovitis were associated more commonly with MACI and ACI. Proud or recessed graft placement is by definition limited to the OAT procedure. In the study by Knutsen et al. [29], the reoperation rate in the ACI group was 25% (10 of 40), whereas it was 10% (four of 40) in the microfracture group.

Discussion

The past 20 years have seen evidence-based medicine play an increasingly important role in physicians' decision making as they determine optimal treatments for their patients. In an evidence-based medicine hierarchy, controlled trials, specifically randomized, controlled trials and controlled, prospective cohort studies, should be weighted most highly in clinical decision making [17, 25, 30, 47]. We have presented data from six Levels I and II studies providing the best data currently available to assess clinical outcomes of advanced cartilage repair techniques relative to each other and to abrasive techniques.

Substantial limitations in the available literature on treatment of full-thickness cartilage defects are apparent in this review. Although data from all of these trials reveal

considerable short-term improvement in all clinical scores with every treatment method evaluated, the lack of a placebo group in these trials limits interpretation of these data to comparisons between treatment methods. The natural history of these defects has been reported in several series, but we were unable to identify any trials comparing operative treatment of the defects with nonoperative management or with simple débridement. One long-term study of 28 minimally treated cartilage defects consisting of 89% partial-thickness defects and 11% full-thickness defects showed fair to poor knee function in 25% at 14 years [31]. Another study of 101 patients with full-thickness defects noted only slightly lower subjective clinical scores and no greater incidence of osteoarthritis at 6 to 9 years when compared with control subjects without cartilage injury [40]. Longer-term followup in the studies included here would allow some comparison to these studies and other historical controls of nonoperative treatment of these defects but still would fall short of a randomized, controlled trial in comparing outcomes. The relatively short followup of all studies identified in this review severely limits interpretation of the data. Any differences in outcome based on the formation of articular rather than fibrocartilage in the defect may be quite subtle and only reveal themselves after many years of followup. Similarly, complications such as donor site morbidity in OAT may be late in their presentation and thus not be detected at short followup. The relatively small number of trials available at the time of this review and the heterogeneity of outcome measures preclude performance of a meta-analysis of the data.

As a result of the above-described limitations in the current literature, we are unable to make a recommendation regarding one superior procedure for all clinical situations. Articular cartilage defects frequently are discovered at arthroscopy and may not be anticipated before the procedure. This situation requires the arthroscopist to make an intraoperative decision regarding the treatment used. The current literature suggests use of any of the treatment methods outlined here results in improved clinical outcome in patients with symptoms, although it is unclear whether this outcome differs from the natural history of these lesions. Microfracture or drilling techniques require little preoperative planning and minimal equipment, and their performance does not preclude performance of OAT or ACI later should symptoms continue. Even in the case of poor patient compliance with postoperative weightbearing limitations, there is a low chance for patient injury. Low morbidity and cost make these techniques ideal first-line treatments for small Stages 3 and 4 articular cartilage defects discovered at arthroscopy. Whether an articular cartilage biopsy for future potential autologous chondrocyte procedure should be obtained depends on several factors, including cost, long-term data, and estimated percentage that would require a second procedure for failed microfracture.

The factors influencing treatment choice for known articular cartilage defects differ in important ways. The disadvantages of OAT and ACI alluded to above, including equipment availability and consent issues, do not apply in this situation. The poorer outcomes of microfracture noted with lesions larger than 2 to 4 cm^2 in two studies may reflect the need for more complex surgery for larger lesions. Specific trials aimed and powered to detect outcome difference between lesion sizes are required to attain a definitive answer. Lesion size and location, expected future activity level, surgeon training and comfort level with specific techniques, and patient preference after informed consent are among the most likely factors considered by surgeons in this decision.

The best way to address the question regarding which treatment method is superior would be a large multicenter trial comparing all four techniques described, simple débridement, and a nonoperative control. This trial should use validated patient-oriented clinical outcome measures, such as the Knee Injury and Osteoarthritis Outcome Score, the WOMAC^{TM} Osteoarthritis Index, SF-36 score, or the International Knee Documentation Committee score, and be continued to obtain longer followup at 5 and eventually 10 years. Until data of this caliber are available, surgeons should base their decision making on their training and experience with different treatment methods, cost-benefit analyses, and patient preference with informed consent regarding the available outcomes data.

Our review of the best available evidence reveals no one technique produces superior clinical results for treatment of full-thickness articular cartilage defects. Microfracture techniques require little preoperative planning and special equipment and failure does not preclude later treatment with ACI or OAT. These factors may influence some surgeons to use microfracture as first-line treatment for articular cartilage defects discovered at arthroscopy. Treatment choice in known lesions requires surgeon interpretation of available data as presented here in light of patient characteristics, lesion location and size, and individual expertise.

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