CARTILAGE
2020, Vol. 11(1) 9–18

DOI: 10.1177/1947603518783503
journals.sagepub.com/home/CAR
SAGE

Articular Cartilage Repair of the Pediatric and Adolescent Knee with Regard to Minimal Clinically Important Difference: A Systematic Review

Rosa S. Valtanen[1], Armin Arshi[1], Benjamin V. Kelley[1], Peter D. Fabricant[2], and Kristofer J. Jones[1]

Abstract

Objective. To perform a systematic review of clinical outcomes following microfracture (MFX), autologous chondrocyte implantation (ACI), osteochondral allograft transplantation (OCA), and osteochondral autograft transplantation system (OATS) to treat articular cartilage lesions in pediatric and adolescent patients. We sought to compare postoperative improvements for each cartilage repair method to minimal clinically important difference (MCID) thresholds. *Design*. MEDLINE, Web of Science, Scopus, and Cochrane Library databases were searched for studies reporting MCID-validated outcome scores in a minimum of 5 patients ≤19 years treated for symptomatic knee chondral lesions with minimum 1-year follow-up. One-sample *t* tests were used to compare mean outcome score improvements to established MCID thresholds. *Results*. Twelve studies reporting clinical outcomes on a total of 330 patients following cartilage repair were identified. The mean age of patients ranged from 13.7 to 16.7 years and the mean follow-up was 2.2 to 9.6 years. Six studies reported on ACI, 4 studies reported on MFX, 2 studies reported on OATS, and 1 study reported on OCA. ACI ($P < 0.001$, $P = 0.008$) and OCA ($P < 0.001$) showed significant improvement for International Knee Documentation Committee (IKDC) scores with regard to MCID while MFX ($P = 0.66$) and OATS ($P = 0.11$) did not. ACI ($P < 0.001$) and OATS ($P = 0.010$) both showed significant improvement above MCID thresholds for Lysholm scores. MFX ($P = 0.002$) showed visual analog scale (VAS) pain score improvement above MCID threshold while ACI ($P = 0.037$, $P = 0.070$) was equivocal. *Conclusions*. Outcomes data on cartilage repair in the pediatric and adolescent knee are limited. This review demonstrates that all available procedures provide postoperative improvement above published MCID thresholds for at least one reported clinical pain or functional outcome score.

Keywords

cartilage injury, pediatric knee, osteochondral allograft, autologous chondrocyte implantation

Introduction

Focal articular cartilage injuries continue to present as challenging clinical problems, particularly when young patients present with large lesions in weight-bearing joints such as the knee. Because of its avascular nature, articular cartilage lacks the ability to spontaneously heal.[1] Furthermore, osteochondral defects that result from displaced osteochondritis dissecans lesions can be particularly problematic as they do not have normal subchondral bone architecture. Chondral and osteochondral lesions can result in significant pain and functional impairment.[2] If left untreated, these lesions can progress to premature knee osteoarthritis, which is particularly problematic in the active pediatric and adolescent population with high functional demands and long life expectancies.[2,3] When nonsurgical management fails, surgical intervention is recommended to restore the articular surface. The surgeon is challenged to address the cartilage lesion in a way that maximizes the integrity of the knee to protect against future degeneration. Advancements in surgical technique

[1]Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
[2]Division of Pediatric Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, USA

Corresponding Author:
Kristofer J. Jones, Department of Orthopaedic Surgery, Division of Sports Medicine and Shoulder Surgery, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, 76-143 CHS, Los Angeles, CA 90095-6902, USA.
Email: kjjonesmd@gmail.com

have provided biological alternatives for the repair of damaged articular cartilage and subchondral bone. These procedures include microfracture (MFX), autologous chondrocyte implantation (ACI), osteochondral allograft transplantation (OCA), and osteochondral autograft transplantation system (OATS).[4]

Despite a myriad of outcomes reports on these techniques, the fundamental weakness of existing literature is the inconsistent use of validated outcome measures, making it difficult to objectively compare the treatment efficacies of these procedures.[5] Indeed, though several surgical options have been proposed based on location, lesion size, and time elapsed since injury, there is no consensus on the ideal indications and outcomes for each procedure. Furthermore, current evidence to guide decision making is mainly in the form of case series rather than prospective randomized controlled trials. When pediatric and adolescent populations are studied alone, even fewer reports are available for comparison to guide treatment decisions. The purpose of this study was to conduct a systematic review of clinical outcomes following MFX, ACI, OCA, and OATS surgery for the treatment of focal knee lesions in pediatric patients. We sought to compare postoperative improvement in functional and activity outcome scores to validated thresholds for minimal clinically important difference (MCID). Our initial hypothesis was that that all available procedures—MFX, ACI, OCA, and OATS—would provide clinically significant improvements in outcomes scores when compared with the current published MCID threshold for each outcome measure.

Materials and Methods

Literature Search

A systematic review was performed using the Web of Science, PubMed, Cochrane Library, and Scopus databases. The review was registered on the PROSPERO database (Registration number: CRD42016052287, University of York, York, United Kingdom). PubMed, Scopus, and Cochrane library databases were searched on December 23, 2015 with the search terms "microfracture" AND "knee." PubMed, Web of Science, and Cochrane library databases were searched on April 12, 2016 with the search terms "((osteochondral autograft transplantation) OR (osteochondral autografting) OR (osteochondral autograft) OR (OC autograft) OR (mosaicplasty) OR (osteoarticular transfer system) OR (osteochondral cylinder transplantation) OR (osteochondral cylinder) OR (autologous chondrocyte implantation) OR (osteochondral allograft) OR (OC allograft)) AND knee." Search terms were general to avoid inadvertent exclusion of relevant studies. Duplicate studies and stand-alone abstracts were excluded. The search algorithm was refreshed on August 25, 2017 to ensure inclusion of all literature published in the interim.

Following the primary search, article titles and abstracts were individually reviewed in accordance with the standard PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. Articles that contained relevant information were identified and systematically analyzed to ensure compliance with the following inclusion criteria: (1) minimum of 5 subjects; (2) pediatric patients aged 19 years and younger; (3) intervention of MFX, ACI, OCA, or OATS; (4) minimum of 1 year of clinical follow-up; (5) clinical outcome reported; and (6) study published in the English language. Review articles, systematic reviews, meta-analyses, cadaveric, *in vitro*, and animal studies were excluded.

Data Abstraction and Statistical Analysis

Studies that met the inclusion/exclusion criteria were independently reviewed and used to extract cohorts of pediatric patients who had undergone MFX, ACI, OCA, and OATS procedures. Reported data on patient age, gender, lesion size, lesion location, number of lesions, presence of prior surgeries and concurrent procedures in the index knee, time between injury and procedure, length of follow-up, as well as pre- and postoperative clinical outcome scores were collected and reviewed. Clinical outcome scores with validated MCID scores included the International Knee Documentation Committee (IKDC), Lysholm, and visual analog scale (VAS) pain scores.[6-8] Two-tailed, 1-sample Student *t* tests were conducted to evaluate for significance of pre- to postoperative mean improvement compared with current MCID thresholds for each individual study. Statistical analyses were performed using SPSS 21 software (IBM Corp., Armonk, NY).

Results

In total, 1,768 articles from PubMed, 156 articles from Cochrane library, 774 articles from Scopus, and 2,084 articles from Web of Science matched our initial search terms, for a total of 4,782 articles. These studies were serially assessed using standardized PRISMA protocol (**Fig. 1**). After duplicates, patents, and published abstracts were removed, 3,102 articles remained for title and abstract review. After application of exclusion criteria, 18 articles remained for full-text review. Of these 18 articles, 4 did not report on subjects younger than 19 years, and 2 did not address a relevant intervention. Twelve articles were included in our review, but 4 articles did not provide sufficient statistics (measure of center and spread for both baseline and final follow-up for IKDC, VAS pain, or Lysholm score) for MCID analysis (**Table 1**). Eight articles were ultimately included for statistical analysis. Four of these studies reported on ACI, 3 reported on MFX, 1 reported on OCA, and 1 reported on OATS. All ACI studies and the

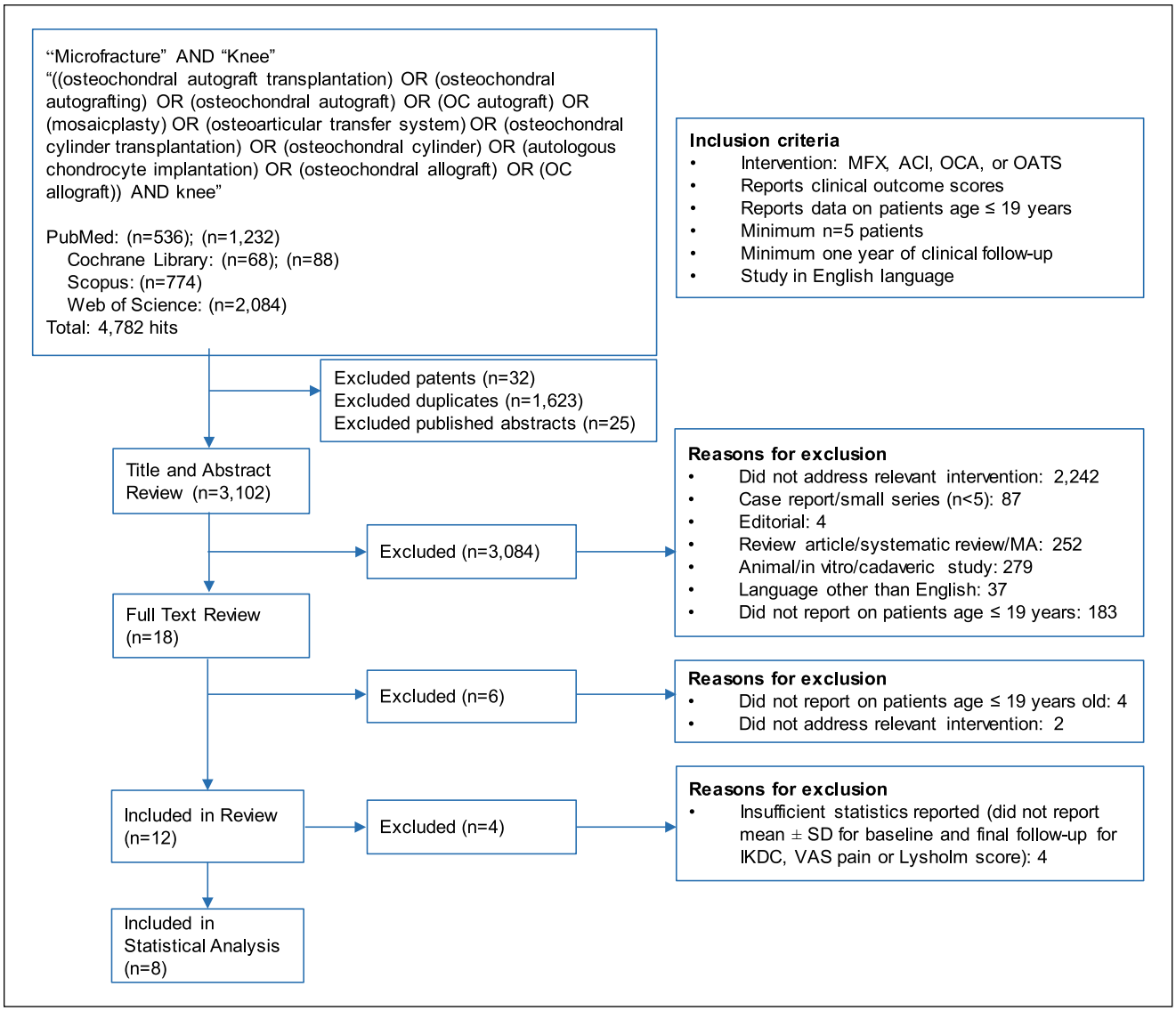

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram outlining the application of the inclusion and exclusion criteria for the systematic review.

OCA study included patients with focal cartilage lesions as well as those resulting from juvenile osteochondritis dissecans (JOCD). The OATS study included only patients with JOCD while the MFX studies did not include any patients with JOCD.

Demographics

Eleven studies were level IV case series and 1 study was a level I randomized controlled trial (RCT). Six studies reported on ACI, 2 studies reported on OATS, 1 study reported on OCA, and 4 studies reported on MFX (Gudas *et al*.[21] reported on 2 procedures, comparing OATS and MFX). There were 330 unique patients identified across all studies; 192 underwent ACI (58.2%), 36 underwent OATS (10.9%), 39 underwent OCA transplantation (11.8%), and 63 underwent MFX (19.1%). Of the entire combined cohort, 58.5% of patients were male. The mean age of all subjects ranged from 13.7 to 16.7 years and mean follow-up ranged from 2.2 to 9.6 years. Average lesion size ranged from 1.2 to 8.4 cm^2 (**Table 1**). Lesions were localized to the medial and lateral femoral condyles, trochlea, patella, and tibial plateau; 251 lesions were condylar (70.1%), 72 were patellar (20.1%), 25 were trochlear (7.0%), and 10 were localized to the tibial plateau (2.8%). Number of lesions treated in each procedure, presence of previous and concurrent surgeries in the index knee, and time between injury and procedure were not uniformly reported across

Table 1. Summary and Characteristics of Studies Identified in Systematic Review.

Study No.	First Author, Year of Publication	*n* (Patients)	Male	Female	Age in Years, Mean (Range)	Lesion Size in cm^2, Mean (Range)	Lesion Location: Condylar (Fc), Patellar (P), Tibial Plateau (Tp), Trochlear (T)	Follow-up in Years, Mean (Range)	Level of Evidence	Level of Evidence, Study Methodology	ACI	OATS	OCA	MFX	IKDC	Lysholm	VAS Pain	Other
1	Cvetanovich, 2017	37	15	22	16.7 (13-18)	4	Fc, P, T	4.6 (2-10.6)	Level IV	Case series	✓				✓			✓
2	Gudas, 2009	25	15	10	14.6 (12-18)	3.2	Fc	4.2 (3-6)	Level I	Randomized controlled trial		✓						✓
2	Gudas, 2009	22	13	9	14.1 (12-18)	3.2	Fc	4.2 (3-6)	Level I	Randomized controlled trial				✓				✓
3	Lee, 2012	5	1	4	14.6 (12-17)	1.2 (1-1.5)	P	2.5 (1.3-4.5)	Level IV	Case series				✓	✓			✓
4	Macmull, 2011	31	22	9	16.3 (14-18)	5.3 (1.0-15.8)	Fc, P, T	5.5 (1-10.5)	Level IV	Case series	✓						✓	✓
5	Micheli, 2006	37	22	15	15.5 (11-17)	5.2 (1.9-14)	Fc	4.3	Level IV	Case series	✓							✓
6	Mithöfer, 2005	20	15	5	15.9 (12-18)	6.4 (2.4-14)	Fc, P, Tp, T	3.9 (1.9-7.6)	Level IV	Case series	✓					✓		✓
7	Murphy, 2014	39	24	15	16.4 (11-17.9)	8.4 (2.2-20.8)	Fc, P, Tp, T	8.4 (1.7-27.1)	Level IV	Case series			✓		✓			✓
8	Niethammer, 2016	40	24	16	16.0 (11-19)	5.3 (1.5-10.5)	Fc, P	3.0	Level IV	Case series	✓				✓		✓	
9	Ogura, 2017	27	13	14	15.9 (13-17)	6.2 (2.0-23.4)	Fc, P, Tp, T	9.6 (2-19)	Level IV	Case series	✓						✓	✓
10	Salzmann, 2012	10	8	2	14.1 (9-16)	1.2	Fc, P, Tp, T	3.5	Level IV	Case series				✓	✓	✓	✓	✓
11	Sasaki, 2012	11	9	2	13.7 (12-16)	2.7 (1-4.5)	Fc	2.2 (0.5-5)	Level IV	Case series		✓			✓	✓		
12	Steadman, 2015	26	12	14	16.6 (12-18.9)	1.9 (0.4-5.7)	Fc, P, T	5.8 (2-13.3)	Level IV	Case series				✓		✓		✓

ACI = autologous chondrocyte implantation; IKDC, International Knee Documentation Committee; MFX = microfracture; OATS = osteochondral autograft transplantation system; OCA = osteochondral allograft transplantation; VAS = visual analogue scale.

Table 2. Lesion Characteristics and Prior and Concomitant Surgeries for Studies Identified in Systematic Review.

Study No.	First Author, Year of Publication	Intervention	*n* (Patients)	Single or Multiple Lesions	No. with Prior Surgeries in Index Knee	No. with Concomitant Procedures in Index Knee
1	Cvetanovich, 2017	ACI	37	Not reported	37/37 patients	22
2	Gudas, 2009	OATS	25	Single lesions	0/25 patients	0
2	Gudas, 2009	MFX	22	Single lesions	0/22 patients	0
3	Lee, 2012	MFX	5	Single lesions	0/5 patients	2
4	Macmull, 2011	ACI	31	30/31 with single lesions; 1/31 with multiple lesions	Mean 1.4 ± 0.6 surgeries per knee	Not reported
5	Micheli, 2006	ACI	37	35/37 with single lesions; 2/37 with multiple lesions	26/37 patients	Not reported
6	Mithöfer, 2005	ACI	20	Mean 1.3 ± 0.3 per knee	Mean 2.5 ± 0.3 surgeries per knee	Not reported
7	Murphy, 2014	OCA	39	35/39 with single lesions; 4/39 with multiple lesions	Mean 1.5 surgeries per knee	15
8	Niethammer, 2016	ACI	40	37/40 with single lesions; 3/40 with multiple lesions	Not reported	Not reported
9	Ogura, 2017	ACI	27	Mean 1.5 ± 1.0 per knee	22/27 patients	22
10	Salzmann, 2012	MFX	10	Single lesions	4/10 patients	Not reported
11	Sasaki, 2012	OATS	11	Single lesions	0/10 patients	Not reported
12	Steadman, 2015	MFX	26	Single and multiple lesions	Not reported	Not reported

ACI = autologous chondrocyte implantation; MFX = microfracture; OATS = osteochondral autograft transplantation system; OCA = osteochondral allograft transplantation.

all studies (**Table 2**). A total of 347 procedures were performed on 330 patients.

Functional Outcome Scores

The most commonly reported outcomes measures were IKDC (6/12), Lysholm (4/12), and VAS pain scores (4/12). Four of these 12 studies were incomplete in reporting data on outcome scores (e.g., mean improvement without measure of spread such as standard deviation, only postoperative score, etc.). Eight studies with 189 unique patients and 202 procedures were included in statistical analysis (**Table 3**). Of these 8 studies, 5 reported complete IKDC scores (2 ACI, 1 MFX, 1 OCA, 1 OATS), two studies reported complete Lysholm outcome scores (1 ACI, 1 OATS), and three studies reported a complete VAS pain outcome score (2 ACI, 1 MFX).

ACI[9,10] ($P = 0.008$, $P < 0.001$) and OCA[11] ($P < 0.001$) showed improvement of IKDC scores above MCID at follow-up; mean improvement in MFX[12] and OATS[13] procedures were not significantly above MCID for IKDC. For Lysholm score, both ACI[14] ($P < 0.001$) and OATS[13] ($P = 0.010$) procedures showed significantly greater improvement relative to known MCID values. MFX[15] ($P = 0.002$) showed significantly greater improvement than MCID with regard to VAS pain score while ACI[10,16] ($P = 0.037$; $P = 0.070$) was equivocal.

Discussion

Most recent reports on the surgical management of articular cartilage lesions focus on adult patients, paralleling the prevalence of these injuries in this population. Pediatric and adolescent patients with articular cartilage defects, though fewer in number, require special attention as these injuries can result in progressive articular cartilage degeneration and functional disability if not properly managed. Common etiologies that cause osteochondral injuries in this patient population include trauma, patellar dislocation, and JOCD. Chondral and osteochondral defects that result from JOCD can be particularly problematic as they do not have normal subchondral bone architecture; thus, traditional MFX or biologically enhanced marrow stimulation techniques may be less effective than in adults. Literature on outcomes following articular cartilage restoration in the pediatric and adolescent population is limited and has not been critically reviewed with regard to objective metrics. This systematic review identified 12 studies and a total of 330 patients reporting clinical outcomes following MFX, ACI, OATS, and OCA for focal lesions of the knee. Here we found that all four of these procedures provided clinically significant improvement in at least one outcomes score when compared to the current published MCID thresholds.[6-8]

Table 3. Statistical Analysis of IKDC, Lysholm, and VAS Pain Score Improvements Compared with MCID.

First Author, Year of Publication	Intervention	*n*	Follow-up in Years, Mean (Range)	Mean Improvement	SD	*P*[a]
IKDC (MCID = 16.7)						
Cvetanovich, 2017	ACI	37	4.6 (2-10.6)	29.7	27.9	0.008*
Niethammer, 2016	ACI	40	3.0	33.7	29.4	<0.001*
Lee, 2012	MFX	5	2.5 (1.3-4.5)	12.2	21.5	0.66
Murphy, 2014	OCA	39	8.4 (1.7-27.1)	33.2	26.1	<0.001*
Sasaki, 2012	OATS	11	2.2 (0.5-5)	24.4	15.4	0.11
Lysholm (MCID = 10.1)						
Mithöfer, 2005	ACI	20	3.9 (1.9-7.6)	23.0	7.6	<0.001*
Sasaki, 2012	OATS	11	2.2 (0.5-5)	21.9	13.2	0.010*
VAS (MCID = 2.7)						
Ogura, 2017	ACI	27	9.6 (2-19)	3.5	2.2	0.080
Niethammer, 2016	ACI	40	3.0	4.0	3.8	0.037*
Salzmann, 2012	MFX	10	3.5	6.2	2.5	0.002*

ACI = autologous chondrocyte implantation; IKDC = International Knee Documentation Committee; MCID = minimal clinically important difference; MFX = microfracture; OATS = osteochondral autograft transplantation system; OCA = osteochondral allograft transplantation; VAS = visual analog scale.
[a]*P* value calculated using 2-tailed, 1-sample Student *t* test.
*$P \leq 0.05$.

Microfracture

At present, MFX is still considered by many to be the "gold standard" procedure for repair of focal articular cartilage defects of the knee. First described by Pridie in 1959 and later refined by Steadman who popularized the technique, MFX is a marrow stimulation technique wherein an awl is used to arthroscopically induce multiple subchondral fractures to facilitate infiltration of blood and stem cells into a local hematoma.[17,18] Theoretically, these stem cells differentiate into fibrocartilage to repair the defect, with the best clinical results seen for patients with lesions <4 cm^2 in size.[19] While it is a cost-effective procedure, MFX does not treat underlying bone defects and has proved less useful in the management of defects that measure greater than 4 cm^2 in size. Similarly, because MFX does not treat abnormal subchondral bone it is less effective for lesions resulting from JOCD.[20] In this review, four articles[12,15,21,22] focused on MFX as an intervention and 2 of these articles[12,15] provided sufficient statistics for MCID analysis. Lee *et al*.[12] retrospectively evaluated the outcomes of five adolescent patients (12-17 years old) who underwent MFX for patellar osteochondral defects (mean size 1.2 cm^2) following patellar dislocation. The time between injury and procedure was not explicitly stated; however, patients who presented greater than 4 weeks from injury were excluded from the study. Though they demonstrated statistically significant improvement in postoperative IKDC scores, the mean improvement did not exceed published MCID thresholds in our independent analysis, likely attributable to an underpowered sample size. In their study, they also found that patients treated with MFX had higher KOOS (Knee injury and Osteoarthritis Outcome Score) and IKDC improvements at short-term when compared with patients treated with open fixation of osteochondral fragments. Salzmann *et al*.[15] conducted a retrospective review to study the clinical outcomes of 10 pediatric patients who underwent MFX for knee articular cartilage defects (mean size 1.2 cm^2). Mean time from injury to operation was 12.1 ± 13.1 months. Lesions were located on the femoral condyles (5/10), patella (2/10), trochlea (2/10), and tibial plateau (1/10). At an average short-term follow-up of 3.5 years, mean improvement in VAS pain was above the published MCID threshold ($P = 0.002$). Compared with adult subjects treated with MFX for osteochondral defects at their institution, they reported significantly greater postoperative improvements in Lysholm, IKDC, and Tegner scores. Patients older than 40 years experienced greater deterioration in postoperative score as compared with younger patients.[23] This difference in outcome may be attributable to decreased quality of cartilage fill resulting from MFX, fibrocartilage rather than hyaline cartilage, paired with a lower regeneration capacity in aging patients.[24]

Steadman *et al*.[22] evaluated the effectiveness of MFX for the treatment of full-thickness chondral knee lesions (mean size 1.9 cm^2) in 26 adolescent patients (28 knees), of whom 22 were available for follow-up at an average of 5.8 years. Eleven patients underwent MFX within 6 months of injury. Lesions were located on the femoral condyles (17/28), patella (10/28), and trochlea (1/28). Mean Lysholm score was 90 (range 50-100), median Tegner scale was 6 (range 2-10), and median patient satisfaction was 10 (range 1-10). One patient required a revision MFX procedure 1-year postoperatively. This study reported insufficient clinical data for MCID analysis in this review.

Autologous Chondrocyte Implantation

ACI is a 2-stage procedure that aims to provide hyaline-like cartilage in a full-thickness articular cartilage lesion using autologous chondrocytes harvested from the patient.[25] This review identified 6 studies[9,10,16,26-28] that focused on ACI as an intervention in the pediatric and adolescent knee; 4 of these studies[9,10,16,28] provided sufficient statistics for MCID analysis.

In their recently published series, Cvetanovich *et al*.[9] reported clinical outcomes following ACI in 37 adolescent patients with a mean lesion size of 4.0 cm^2 and mean follow-up of 4.6 years. The time between injury and ACI was not reported. Lesions were located on the femoral condyles (23/37), patella (7/37), and trochlea (7/37). At final follow-up, mean improvement in IKDC was 29.7 points and mean improvement in KOOS–Quality of Life was 31.0 ($P < 0.001$). In our statistical analysis, IKDC scores showed significant improvement relative to MCID following ACI ($P = 0.008$). Of note, the authors reported that 14 of the 37 patients (37.8%) required 1 to 3 subsequent surgeries after ACI, including debridement for graft hypertrophy (54%), meniscectomy (11%), MFX (9%), and loose body removal (9%). In the adult population, reoperation rate averages 37%; however, the indication for reoperation differs: 35% not related to original defect, 29% lysis of adhesions, 19% knee arthroplasty, 19% revision cartilage operation, 6% to 39% graft hypertrophy.[29] Reoperation following ACI in young patients may be attributable to a more robust response to graft incorporation as compared with adults. Overall, the reoperation rate for ACI is substantially higher than that reported in the MFX literature.

Mithöfer *et al*.[28] evaluated the clinical efficacy of ACI in the management of full-thickness articular cartilage lesions (mean size 6.4 cm^2) of the knee in 20 adolescent athletes (23 knees, average 1.3 lesions per knee). Lesions were located on the femoral condyles (20/27), patella (1/27), trochlea (4/27), and tibial plateau (2/27). The mean time from injury to ACI was 21 ± 17 months. At an average follow-up of 3.9 years, mean improvement in Lysholm score was above the established MCID ($P < 0.001$). Of note, 96% of patients were routinely engaged in high-impact aerobic sports at a recreational level or higher at follow-up. In their 2016 study, Niethammer *et al*.[10] studied clinical results of ACI in the treatment of full-thickness chondral knee lesions (mean size 5.3 cm^2) in 40 children and adolescents (43 knees) with 3-year follow-up. Cartilage defects were the result of OCD in 13 patients, acute trauma (<12 months from injury) in 9 patients, old trauma (>12 months from injury) in 5 patients, and of unclear etiology in 13 patients. Lesions were located on the femoral condyles (17/43) and patella (26/43). In our statistical analysis, ACI[10] showed significant improvement in both IKDC ($P < 0.001$) and VAS pain scores ($P = 0.037$) with regard to MCID. Ogura *et al*.[16] reviewed clinical outcomes of 27 adolescents (29 knees, average 1.5 lesions per knee) undergoing ACI for knee articular cartilage defects (mean size 6.2 cm^2). Mean duration of symptoms prior to ACI was 3.3 years. Lesions were located on the femoral condyles (18/40), patella (10/40), trochlea (6/40), and tibial plateau (6/40). At an average follow-up of 9.6 years, mean improvement in VAS pain score was 3.5 ± 2.2 ($P = 0.070$). While they demonstrated statistically significant improvement in VAS pain scores, the mean improvement did not exceed published MCID thresholds in our independent analysis. Of note, 20 knees required a total of 29 subsequent procedures; 44.8% (13/29) were graft-related while 55.2% (16/29) were unrelated to the graft. Graft-related complications were more common with the use of periosteum (76.9%) as compared with Bio-Gide (23.1%). The overall failure rate was 20% (4/20). Failure was defined as unresolved or recurrent symptoms paired with MRI confirmation of graft delamination, surgical debridement of more than 25% of graft area, or a second cartilage restoration procedure, including revision ACI, MFX, and autologous bone grafting.

Though they reported insufficient statistical data to perform MCID analysis, 2 other ACI studies deserve mention. Micheli *et al*.[27] noted that 6 of 37 patients (mean size 5.2 cm^2) required a revision operation following ACI, and one additional patient had graft failure due to infection and was treated with MFX. Time between injury and ACI was not reported. In their series of 31 patients (mean size 5.3 cm^2), Macmull *et al*.[26] reported 1 failure at 4 years following ACI, which was revised with matrix-assisted chondrocyte implantation (MACI), and another patient who had symptomatic periosteal graft hypertrophy that required arthroscopic debridement. Mean time between injury and ACI was 43 months. The average lesion size among the 6 ACI studies was 5.4 cm^2. From this body of literature, we conclude that while ACI surpasses published MCID thresholds in postoperative clinical improvement, there is a notably high rate of complications and reoperations in the pediatric/adolescent cohort. While reported reoperation rates are comparable between pediatric and adult populations, 37.8% and 37%, respectively, the majority of pediatric complications are due to graft hypertrophy whereas adult complications are more often unrelated to the initial operation or associated with graft failure.[9,29]

Osteochondral Allograft Transplantation

OCA transplantation procedures have become increasingly popular for the treatment of large, focal cartilage defects. The goal of OCA is to transplant a size-matched fresh donor allograft, with viable chondrocytes and underlying subchondral bone, into a socket drilled at the site of the recipient's defect. Advantages of this procedure include the ability to address abnormal subchondral bone and to treat

large defects. The notable disadvantage is that fresh allograft is expensive and in limited supply, which can lead to prolonged surgical delays. One study[11] focused on OCA as an intervention and provided sufficient statistics for MCID analysis. In this study, Murphy *et al*.[11] reported a case series to evaluate OCA graft survivorship in 39 pediatric patients (43 knees) with large osteochondral defects (mean size 8.4 cm^2) at an average follow-up of 8.4 years. The time between injury and OCA was not reported. Lesions were located on the femoral condyles (33/39), patella (3/39), trochlea (2/39), and tibial plateau (1/39). Mean improvement in IKDC score at an average follow-up of 8.4 years was 33.2 ± 26.1. At a median of 2.7 years, 5 grafts had failed. Four of these were successfully managed with a second OCA, while 1 patient underwent total knee arthroplasty after attempted revision OCA approximately 8.6 years after the initial procedure. The authors report a 90% graft survivorship at 10 years and an 88% good/excellent (18-point scale) patient rating at final follow-up. In our statistical analysis, OCA[11] showed significant improvement relative to MCID for the IKDC score ($P < 0.001$).

Osteochondral Autograft Transplantation System

OATS/mosaicplasty involves removing osteochondral bone plugs from an unaffected, low-weight bearing region of the patient's own knee and transplanting it into the defect location.[19] Donor site morbidity imposes size constraints for this procedure, which is preferably used for medium-sized lesions (2.5-4 cm^2).[19] As with OCA, the radius of curvature of the graft and defect location must be closely matched as incongruity can compromise graft survival due to increased contact pressure.[30] Because it is autologous tissue, OATS does not carry the same risk of disease transmission as OCA. Furthermore, OATS is a cost-effective procedure that can be performed during a single open or arthroscopic procedure. Two studies[13,21] reported on OATS in the pediatric and adolescent population, one of which[13] provided sufficient statistics for MCID analysis; the other[21] was an RCT comparing MFX and OATS.

Sasaki *et al*.[13] investigated clinical outcomes of OATS surgery in patients with JOCD. Eleven unique patients with an average lesion size of 2.7 cm^2 underwent 12 OATS procedures for condylar lesions. Mean time from symptom onset to OATS was 13.5 months. At an average follow-up of 2.2 years, observed mean improvement in IKDC score and Lysholm score were 24.4 ± 15.4 and 21.9 ± 13.2, respectively. OATS[13] showed postoperative improvements significantly greater than the published Lysholm MCID score ($P = 0.010$), while IKDC scores were not.

The only RCT identified in this review was published by Gudas *et al*.,[21] comparing MFX and OATS as treatment for JOCD defects of the femoral condyles (mean size 3.2 cm^2). Mean time from symptom onset to operation was 23.5 ± 4.2 months. International Cartilage Repair Society (ICRS) functional and objective evaluation showed that both OATS and MFX groups had significant clinical improvement ($P < 0.05$) after 1 year, and maintained significant clinical improvement compared with pretreatment values after 4.2 years. At the 1-year follow-up, 23/25 (92%) patients had excellent or good results following OATS procedure while 19/22 (86%) patients had excellent or good results following the MFX procedure. At mean follow-up of 4.2 years, 19/23 (86%) patients who underwent the OATS procedure maintained excellent or good results as compared with 12/19 (63%) patients who underwent the MFX procedure. There were no failures in the OATS cohort while the failure rate in the MFX group was 41% (9/22 patients) at follow-up.

While this review identifies a series of 12 studies that have documented clinical outcomes of pediatric and adolescent patients that underwent MFX, ACI, OCA, and OATS procedures, the literature remains nonstandardized in its reporting of specific clinical outcome scores.[31] This makes the objective comparison of results from different studies near impossible, thereby complicating clinical decision making. Small sample sizes in the remaining studies further complicate analysis by limiting the power of statistical tests. Specific guidelines for the reporting of clinical outcome scores, consistent among all studies, should be established to ensure the ability to compare results with one another. We also note the lack of high-quality level I or II studies (only 1 identified in this review) that would most reliably help guide clinical decision making.[32] Finally, the literature is heterogeneous in reporting the etiology of osteochondral lesions of the knee, which is an important consideration given that JOCD has a distinct pathophysiology, natural history, and outcome compared with acute traumatic cartilage injuries.

In summary, our results demonstrate that all available cartilage restoration procedures (MFX, ACI, OCA, and OATS) are effective surgical treatments for pediatric and adolescent patients with symptomatic articular cartilage lesions of the knee. Of note, MFX lesions were on average smaller than ACI, OATS, and OCA lesions (1.9 cm^2, 5.4 cm^2, 3.0 cm^2, and 8.4 cm^2, respectively). Additionally, 61/63 MFX lesions were single and only 4/63 patients (6.3%) had prior surgery in the index knee at the time of operation. From this, we conclude that if MFX was performed, it was likely to be applied as first-line treatment for smaller osteochondral lesions. These procedures all provide significant postoperative improvement in functional and activity outcome scores relative to validated MCID. Head-to-head RCTs and larger case series reporting consistent validated outcomes measures are needed to guide clinical decision making in young patients, particularly ones that distinguish between traumatic chondral defects and osteochondral defects resulting from JOCD. Currently, no consensus exists for optimal treatment of articular cartilage

lesions in the pediatric population, with algorithms being primarily surgeon specific.

Authors' Note

This study was primarily performed at the Department of Orthopedic Surgery in the David Geffen School of Medicine at UCLA.

Acknowledgments and Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ORCID iD

Armin Arshi https://orcid.org/0000-0002-3391-551X

References

1. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee: average 11-year follow-up. Arthroscopy. 2003;19(5):477-84.
2. Bedi A, Feeley BT, Williams RJ 3rd. Management of articular cartilage defects of the knee. J Bone Joint Surg Am. 2010;92(4):994-1009.
3. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med. 2000;133(5):321-8.
4. Cole BJ, Pascual-Garrido C, Grumet RC. Surgical management of articular cartilage defects in the knee. J Bone Joint Surg Am. 2009;91(7):1778-90.
5. Harris JD, Erickson BJ, Abrams GD, Cvetanovich GL, McCormick FM, Gupta AK, *et al*. Methodologic quality of knee articular cartilage studies. Arthroscopy. 2013;29(7):1243-1252.e5.
6. Badalà F, Nouri-mahdavi K, Raoof DA. NIH public access. Computer (Long Beach Calif). 2008;144(5):724-32.
7. Irrgang J. Summary of Clinical Outcome Measures for Sports-Related Knee Injuries. Final Report. Rosemont, IL: AOSSM Outcomes Task Force; 2012:1-381.
8. Katz NP, Paillard FC, Ekman E. Determining the clinical importance of treatment benefits for interventions for painful orthopedic conditions. J Orthop Surg Res. 2015;10:24.
9. Cvetanovich GL, Riboh JC, Tilton AK, Cole BJ. Autologous chondrocyte implantation improves knee-specific functional outcomes and health-related quality of life in adolescent patients. Am J Sports Med. 2017;45(1):70-6.
10. Niethammer TR, Holzgruber M, Gülecyüz MF, Weber P, Pietschmann MF, Müller PE. Matrix based autologous chondrocyte implantation in children and adolescents: a match paired analysis in a follow-up over three years post-operation. Int Orthop. 2017;41(2):343-50.
11. Murphy RT, Pennock AT, Bugbee WD. Osteochondral allograft transplantation of the knee in the pediatric and adolescent population. Am J Sports Med. 2014;42(3):635-40.
12. Lee BJ, Christino MA, Daniels AH, Hulstyn MJ, Eberson CP. Adolescent patellar osteochondral fracture following patellar dislocation. Knee Surg Sports Traumatol Arthrosc. 2013;21(8):1856-61.
13. Sasaki K, Matsumoto T, Matsushita T, Kubo S, Ishida K, Tei K, *et al*. Osteochondral autograft transplantation for juvenile osteochondritis dissecans of the knee: a series of twelve cases. Int Orthop. 2012;36(11):2243-8.
14. Mithoefer K, Williams RJ 3rd, Warren RF, Potter HG, Spock CR, Jones EC, *et al*. The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. J Bone Joint Surg Am. 2005;87(9):1911-20. doi:10.2106/JBJS.D.02846.
15. Salzmann GM, Sah BR, Schmal H, Niemeyer P, Sudkamp NP. Microfracture for treatment of knee cartilage defects in children and adolescents. Pediatr Rep. 2012;4(2):e21.
16. Ogura T, Bryant T, Minas T. Long-term outcomes of autologous chondrocyte implantation in adolescent patients. Am J Sports Med. 2017;45(5):1066-74.
17. Pridie KH. A method of resurfacing osteoarthritic knee joints. J Bone Joint Surg Am. 1959;41:618-9.
18. Steadman JR, Rodkey WG, Singleton SB, Briggs KK. Microfracture technique for full-thickness chondral defects: technique and clinical results. Oper Tech Orthop. 1997;7(4):300-4.
19. Falah M, Nierenberg G, Soudry M, Hayden M, Volpin G. Treatment of articular cartilage lesions of the knee. Int Orthop. 2010;34(5):621-30.
20. Sanders TL, Pareek A, Obey MR, Johnson NR, Carey JL, Stuart MJ, *et al*. High rate of osteoarthritis after osteochondritis dissecans fragment excision compared with surgical restoration at a mean 16-year follow-up. Am J Sports Med. 2017;45(8):1799-1805.
21. Gudas R, Simonaityte R, Cekanauskas E, Tamosiūnas R. A prospective, randomized clinical study of osteochondral autologous transplantation versus microfracture for the treatment of osteochondritis dissecans in the knee joint in children. J Pediatr Orthop. 2009;29(7):741-8.
22. Steadman JR, Briggs KK, Matheny LM, Guillet A, Hanson CM, Willimon SC. Outcomes following microfracture of full-thickness articular cartilage lesions of the knee in adolescent patients. J Knee Surg. 2015;28(2):145-50.
23. Kreuz PC, Erggelet C, Steinwachs MR, Krause SJ, Lahm A, Niemeyer P, *et al*. Is microfracture of chondral defects in the knee associated with different results in patients aged 40 years or younger? Arthroscopy. 2006;22(11):1180-6.
24. Verbruggen G, Cornelissen M, Almqvist KF, Wang L, Elewaut D, Broddelez C, *et al*. Influence of aging on the synthesis and morphology of the aggrecans synthesized by differentiated human articular chondrocytes. Osteoarthritis Cartilage. 2000;8(3):170-9.
25. Brittberg M, Faxén E, Peterson L. Carbon fiber scaffolds in the treatment of early knee osteoarthritis. A prospective

4-year followup of 37 patients. Clin Orthop Relat Res. 1994;(307):155-64.
26. Macmull S, Parratt MTR, Bentley G, Skinner JA, Carrington RWJ, Morris T, *et al*. Autologous chondrocyte implantation in the adolescent knee. Am J Sports Med. 2011;39(8):1723-30.
27. Micheli LJ, Moseley JB, Anderson AF, Browne JE, Erggelet C, Arciero R, *et al*. Articular cartilage defects of the distal femur in children and adolescents: treatment with autologous chondrocyte implantation. J Pediatr Orthop. 2006;26(4):455-60.
28. Mithöfer K, Minas T, Peterson L, Yeon H, Micheli LJ. Functional outcome of knee articular cartilage repair in adolescent athletes. Am J Sports Med. 2005;33(8):1147-53.
29. Pareek A, Carey JL, Reardon PJ, Peterson L, Stuart MJ, Krych AJ. Long-term outcomes after autologous chondrocyte implantation : a systematic review at mean follow-up of 11.4 years. Cartilage. 2016;7(4):298-308.
30. Patil S, Butcher W, D'Lima DD, Steklov N, Bugbee WD, Hoenecke HR. Effect of osteochondral graft insertion forces on chondrocyte viability. Am J Sports Med. 2008;36(9): 1726-32.
31. Jones KJ, Sheppard WL, Arshi A, Hinckel BB, Sherman SL. Articular cartilage lesion characteristic reporting Is highly variable in clinical outcomes studies of the knee. Cartilage. Epub 2018 February 6. doi:10.1177/1947603518756464.
32. Arshi A, Siesener NJ, McAllister DR, Williams RJ 3rd, Sherman SL, Jones KJ. The 50 most cited articles in orthopedic cartilage surgery. Cartilage. 2016;7(3): 238-47.