



Cartilage Restoration in the Adolescent Knee: a Systematic Review

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Abstract

Purpose of Review The purpose of this systematic review was to assess the outcomes and complications of described cartilage restoration techniques for cartilage defects (grades I to IV) in the adolescent knee.

Recent Findings Eleven studies satisfied the inclusion criteria comprising 307 patients with a mean follow-up of 4.6 years (range 1–18.9 years). Study patients were treated with autologous chondrocyte implantation (ACI) ($n = 98$, mean age 16.0), microfracture (MFx) ($n = 36$, mean age 15.4), internal fixation ($n = 71$, mean age 13.1), osteochondral allograft (OCA) transplantation ($n = 78$, mean age 16.4), and cartilage and excision ($n = 24$; mean age 14.2). ACI, MFx, OCA transplantation, and internal fixation showed significant improvement in knee functionality scores. The overall complication rate was 10.6% ($n = 31$). OCA transplantation had the highest complication rate (26.9%; $n = 21/78$).

Summary In summary, our review shows that ACI was the most commonly used technique. Furthermore, ACI, MFx, OCA transplantation, and internal fixation show the most promise in treating the adolescent population due to positive postoperative functional outcomes and low complication rates. However, future studies with large sample sizes, standardized outcome documentation, and long-term follow-up are required to confirm these preliminary results.

Keywords Adolescent · Knee · Cartilage · OCD · Patella

Introduction

Chondral defects in the knees of adolescent patients are prevalent for multiple reasons, ranging from osteological disorders to acute trauma, especially with increasing participation in sports [1•, 2, 3]. Full-thickness chondral/osteochondral articular defects from osteochondritis dissecans (OCD) alone can affect up to 15 to 30 in 100,000 adolescent patients [1•, 2]. Therefore, appropriately

treating chondral lesions in adolescent populations is important to prevent or slow long-term complications such as osteochondral refractures or premature osteoarthritis [1•, 2].

Compared to adults, the adolescent population shows more promise in the treatment of such chondral defects given their increased potential for cellular differentiation and proliferation [1•, 2]. Particularly, the relatively increased capacity for chondral injury healing may capitalize upon various available treatment options to allow for better outcome in treatment of chondral defects [1•, 2]. However, given the overall limited capacity of hyaline cartilage regeneration, it is necessary to determine an appropriate method of treatment to maximize outcomes in such a young population. There is a wide array of cartilage restoration techniques available to the adolescent population (less than 19 years of age) to treat these chondral defects [1•, 2]. Abrasion arthroplasty, drilling, and microfracture (MFx) are options whereby underlying bone marrow is stimulated for fibrocartilage repair. Likewise, autologous chondrocyte implantation (ACI) is a newer option in which a chondrocyte scaffold is used to initiate chondral repair, which is more hyaline-like. Recent systematic reviews investigating the utility of ACI have found it to be an extremely safe and effective method [1•, 2].

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More specifically, studies have shown its benefit in the treatment of large cartilage lesions in adolescent patients due to their regenerative capacity [1•, 4].

Mosaicplasty uses autografts or allografts from cadaveric donors to treat chondral defects [1•, 2]. However, graft mismatching is an inherent risk with this technique. Mosaicplasty is typically only utilized in larger chondral defects (i.e., 2 cm²) [1•, 2]. Internal fixation of intact, full-thickness chondral defects involves reduction of chondral fragments; excellent radiologic and clinical outcomes have been observed previously [5].

There is an increasing interest in the treatment of this challenging clinical problem via cartilage restoration. The objective of this systematic review was to identify trends, outcomes, and complications of various cartilage restoration techniques for full-thickness cartilage defects in the adolescent knee. It was hypothesized that all identified cartilage restoration techniques will yield similar long-term outcomes and that ACI will be the most commonly used restoration technique.

Methods

This systematic review was completed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Revised Assessment of Multiple Systematic Reviews (R-AMSTAR) [6, 7].

Study Screening

A systematic screening approach was employed from title to full-text screening stages in duplicate by two independent reviewers [8]. Discrepancies were discussed and resolved with input by a third reviewer. The references of included studies were also screened using the same systematic approach to capture any additional relevant articles.

Search Strategy

Two independent reviewers searched EMBASE and MEDLINE (including Epub Ahead of Print articles) for the literature on cartilage restoration techniques to treat full-thickness cartilage defects in the knee from January 1946 to January 15, 2019. The search terms included “articular cartilage,” “adolescent,” “chondropathy,” and similar phrases (Table 3). The research question and inclusion and exclusion criteria were established a priori. Inclusion criteria included the following: (1) all levels of evidence, (2) patients aged \leq 19 years [5], (3) studies primarily focusing on focal cartilage defects (grades I–IV) of the knee (all compartments, i.e., tibiofemoral, patellofemoral), (4) cartilage restoration technique(s) used (ACI, MFx, osteochondral allograft (OCA) transplantation, etc.), (5) surgical outcomes reported, (6) human subjects, and (7) $>$ 5 patients. The exclusion criteria

included (1) osteoarthritis, (2) inflammatory arthritis, (3) associated ligamentous injury, (4) cadaver/non-human studies, (5) review articles, and (6) non-surgical treatment studies (e.g., conservative treatment and technique articles without outcomes).

Quality Assessment

Using the *Journal of Bone and Joint Surgery (JBJS)* classification system for the literature in the field of orthopedics, the level of evidence (I to IV) for each study was determined by the two reviewers independently and in duplicate [7]. The methodological quality of non-randomized comparative studies was evaluated using the Methodological Index for Nonrandomized Studies (MINORS) [9]. A score of 0, 1, or 2 is given for each of the 12 items on the MINORS checklist with a maximum score of 16 for non-comparative studies and 24 for comparative studies. Methodological quality was categorized a priori as follows: a score of 0–8 or 0–12 was considered poor quality, a score of 9–12 or 13–18 was considered fair quality, and a score of 13–16 or 19–24 was considered excellent quality, for non-comparative and comparative studies, respectively.

Data Abstraction

Two reviewers independently abstracted relevant data from included articles. Demographic data included author, year of publication, sample size, study design and location, level of evidence, and patient demographics (e.g., gender and age). Information regarding postoperative outcomes (surgical and radiographic) and complications was documented.

Statistical Analysis

Due to the high statistical and methodological heterogeneity and lack of higher-quality comparative studies, a meta-analysis could not be performed. The results are summarized descriptively. Descriptive statistics such as mean, range, and measures of variance (e.g., standard deviations and 95% confidence intervals (CIs)) are presented where applicable. The intraclass correlation coefficient (ICC) was used to evaluate inter-reviewer agreement for the quality assessment. A kappa (κ) statistic was used to evaluate inter-reviewer agreement at all screening stages. Agreement was categorized a priori as follows: an ICC/ κ value of 0.81 to 0.99 was considered as almost perfect agreement, an ICC/ κ value of 0.61 to 0.80 was substantial agreement, an ICC/ κ value of 0.41 to 0.60 was moderate agreement, an ICC/ κ of value 0.21 to 0.40 was fair agreement, and a ICC/ κ value of 0.20 or less was considered slight agreement [10].

Results

Study Characteristics

The initial search of online databases yielded a total of 4680 articles. After excluding 1290 duplicates, the systematic screening process identified eleven articles that satisfied the inclusion and exclusion criteria (Fig. 1). There was substantial agreement among reviewers at the title ($\kappa = 0.865$ (95% CI 0.841 to 0.889)), abstract ($\kappa = 0.650$ (95% CI 0.593 to 0.706)), and full-text ($\kappa = 0.761$ (95% 0.685 to 0.837)) screening stages.

Study Quality

The 11 included studies comprised of 8 case series, 2 case-control studies, and 1 retrospective cohort. The majority of included studies were of level IV evidence (63.6%; $n = 7$). The mean MINORS score for non-comparative studies was

11.2 ± 0.4 indicating poor quality of evidence, and that for comparative studies was 18.0 indicating fair quality of evidence with only one presenting an adequate statistical analysis ($n = 1/11$; 9.1%) and one studying having baseline equivalence of groups ($n = 1/11$; 9.1%). Based on the MINORS scoring criteria, the top 3 strengths with respect to adequate reporting were clearly stated aim ($n = 11/11$; 100%), appropriate follow-up period ($n = 11/11$; 100%), and end points appropriate for the aim ($n = 11/11$; 100%). There was near-perfect agreement among the reviewers for the quality assessment using the MINORS criteria (weighted ICC = 0.962; 95% CI 0.945 to 0.973) (Table 1).

Patient Characteristics

In this systematic review, there were 307 patients (320 defects) with a mean age of 13.1 years (range, 9.0 to 18.9) of which 48.9% ($n = 150$) were male. Patients had a mean follow-up of 4.6 years with a reported range of 1–27.1 years. Seven studies

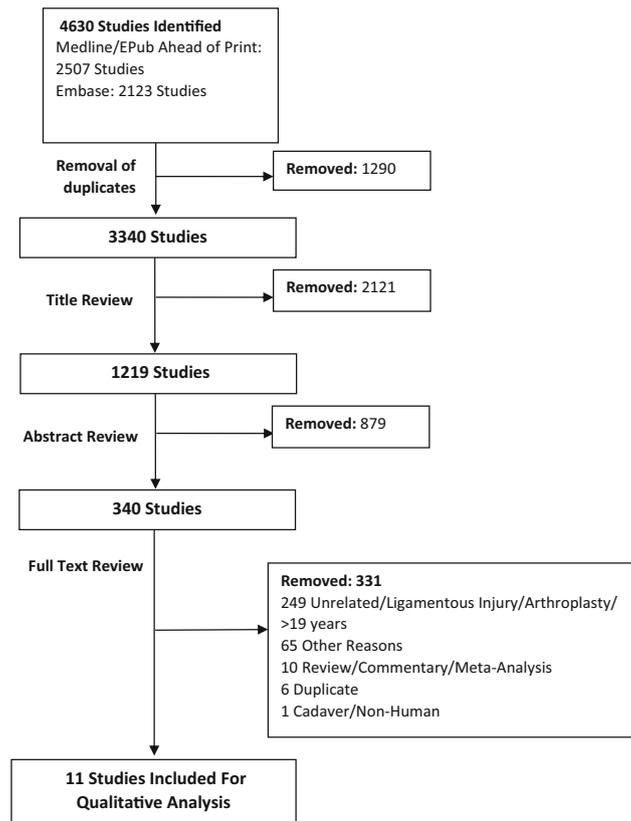


Fig. 1 PRISMA flow diagram

Table 1 Study characteristics and demographics

Authors (year)	Study design (level of evidence)	MINORS score	Number of patients (defects)	% male	Skeletal maturity	Follow-up time (range), years	Mean age (range), years	Country of publication
Niethammer et al. (2017)	Case-control (III)	15/24	40 patients (43 defects) Control = 40 patients	60% Comparison = 62.5%	NR	3 years Comparison = 3 years	16 years SD (2.06) Comparison = 36.7 years SD (8.2)	Germany
Ogura et al. (2017)	Case series (III)	11/16	27 patients (29 defects)	48%	Immature (9) Mature (18)	9.6 years (2–19)	15.9	USA
Steadman et al. (2015)	Case series (IV)	11/16	26 patients	46%	NR	5.8 years (2–13.3)	16.6 (12–18.9)	USA
Murphy et al. (2014)	Case series (IV)	12/16	39 patients (43 defects)	61%	NR	8.4 years (1.7–27.1)	16.4 (11–17.9)	USA
Pennoek et al. (2013)	Case series (IV)	11/16	39 patients (43 defects)	61%	NR	8.4 years (1.7–27.1)	16.4 (11–17.9)	USA
Chotel et al. (2011)	Case series (IV)	11/16	14 patients	50%	Immature (14)	2.5 years	13.5 (11.2–15)	France
Schmal et al. (2010)	Case-control (III)	11/16	23 patients	74%	NR	3.3 years	12.4	Germany
Macmull et al. (2011)	Case series (IV)	12/16	31 patients	71%	NR	5.5 years (1–10.5)	16.3 (14–18)	UK
Salzmann et al. (2012)	Case series (IV)	11/16	10 patients	80%	NR	3.5 years	14.1 years	Germany
Kang et al. (2018)	Retrospective cohort (III)	18/24	19 patients Comparison = 24 patients	42%	NR	2.1 years Comparison = 2.6 years	13.9 years	China
Fabricant et al. (2018)	Case series (IV)	11/16	15 patients	73%	Immature = 14 Mature = 1	1 year	Comparison = 14.2 years 12.7 years	USA

reported chondral-only defect lesion sizes with a mean defect size of 5.1 cm² (range 2 to 8.4). Three studies ($n = 56$) reported skeletal maturity based on the status of the epiphyseal growth plate. Of those patients, 37 (66%) were skeletally immature. Nine studies ($n = 270$) comprising 294 defects reported defect location (Table 2). These comprised of the patella ($n = 73$ defects), medial femoral condyle ($n = 51$ defects), lateral femoral condyle ($n = 43$ defects), trochlea ($n = 11$ defects), lateral tibial plateau ($n = 6$ defects), medial tibial plateau ($n = 1$ defect), and multiple locations (4 defects). One study reported 17 femoral defects without specifying if they were trochlear or condylar. There were an additional 33 femoral condyle defects reported that did not specify whether they were medial or lateral. Finally, four studies that reported tibial plateau defects did not specify a location. The etiologies of the full-thickness articular cartilage defects were 83 osteochondritis dissecans, 160 trauma, 34 degenerative, 72 chondromalacia patella, 1 osteomyelitis, and 2 unknown. There was insufficient information regarding grade of full-thickness articular cartilage defects.

Surgical Techniques

Study patients were treated with ACI (31.8%; $n = 98$, mean age 16.0), OCA transplantation (25.3%; $n = 78$, mean age 16.4), internal fixation (23.1%; $n = 71$, mean age 13.1), MFX (11.9%; $n = 36$, mean age 15.4), and cartilage and excision (7.8%; $n = 24$, mean age 14.2) (Table 2). Of the internal fixation studies that reported fixation implants, fixation implants included bioabsorbable tacks alone ($n = 8$), tacks and screw ($n = 1$), tacks/screw and suture ($n = 3$), sutures alone ($n = 1$), sutures with suture anchor ($n = 1$), and tacks and suture with suture anchors ($n = 1$). Lesion sizes were reported in Table 2.

Outcomes

Radiographic Outcomes

Radiographic outcomes were only reported in 1 study. In the internal fixation group ($n = 71$), 56% ($n = 5/9$) of measured patients showed satisfactory cartilage restoration via MRI examination (median 12.0 months postoperatively) [11].

Knee Functionality

In the OCA transplantation group ($n = 78$), mean International Knee Documentation Committee (IKDC) scores significantly increased in 100% ($n = 78$) of patients ($p < 0.05$). Additionally, KS-F scores significantly increased in 100% ($n = 78$) of patients ($p < 0.05$). In 100% ($n = 39$) of measured patients, based on the modified Merle d'Aubigné-Postel scale, 87.5% of patients had a “good” or “excellent” score postoperatively [12, 13] (Table 2).

In the ACI group ($n = 98$), the mean subjective IKDC score significantly increased postoperatively in 100% ($n = 40$) of measured patients ($p = 0.002$) and Cincinnati Knee Rating Scale scores significantly increased in 100% ($n = 57$) of measured patients ($p < 0.05$) [14–16] (Table 2).

In the internal fixation group ($n = 71$), the mean subjective IKDC score significantly increased in 100% of patients ($n = 37$) ($p < 0.05$). Additionally, 56.7% ($n = 21$) of measured patients noted at least a “good” HSS score [17, 18] (Table 2).

Return to Sport

Return to sport was measured in only 1 study ($n = 15$). All of these patients returned to sport at a satisfactory level [11].

Complications and Revision Rates

The overall complication rate was 10.6% ($n = 31$). Complication rates were reported based on the populations of individual techniques: OCA transplantation (26.9%, $n = 21/78$), internal fixation (12.7%; $n = 9/71$), and ACI (1.0%, $n = 1/98$). OCA transplantation had the highest revision rate (26.9%, $n = 21/78$), of which the most common reasons were diagnostic arthroscopy ($n = 6$), loose body removal ($n = 4$), and chondroplasty ($n = 3$). Internal fixation had a revision rate of 4.2% ($n = 3/71$) [12–16].

Discussion

The most important finding of this systematic review was that all techniques yielded similar outcomes at a short-term follow-up with ACI being the most commonly used restoration technique. These findings are consistent with a recent systematic review on cartilage restoration in the adult population [19••]. Additionally, OCA transplantation, internal fixation, and ACI had the highest complication rates, respectively. OCA transplantation and internal fixation had the highest revision rates, respectively.

The adolescent population generally presents with some important differences with respect to adults which can affect their outcomes. Particularly, given their younger age, it has been proposed that adolescent patients’ epiphyseal chondrocytes have greater growth factor expression allowing for improved chondral restoration (which otherwise has extremely limited restorative capacity) [1, 2, 20]. However, in spite of this potential, adolescent patients are more susceptible to lesions that last for long periods of time which may impair chondral function [1, 2, 19••]. Thus, these factors emphasize the need to repair and preserve cartilage in adolescent patients to maximize long-term outcomes [1, 2, 20].

It has been previously noted that techniques leading to successful outcomes in the short term have better long-term

outlook compared to those with poorer short-term outcomes [1, 2, 20]. Subsequently, it is not surprising that in the current review, ACI, MFx, internal fixation, and OCA transplantation showed the best improvement in knee functionality. All of these techniques use different methodologies to restore chondral lesions which translate into better long-term outcomes [1, 2, 20]. Moreover, various studies have found that techniques such as ACI capitalize on this capacity effectively which leads to greater success in restoring functionality in the adolescent population, as compared to adult age-matched controls [1, 2, 20]. In OCA transplantation patients, age has been said to have a significant impact on successful outcomes such that younger patients are more likely to have successful outcomes [21]. A systematic review evaluating MFx, ACI, and OCA transplantation in a similar population affirmed the success of these results [22•]. Similarly, there still is a dearth of evidence available to determine a superior technique [19••].

Interestingly, despite the claim that adolescent patients have a better chance for success, the current review noted a high revision rate for patients treated with OCA transplantation. Successful OCA transplantation is dependent upon the successful integration of the allograft in the host; however, this is influenced by several factors including graft type, location of the defect, immunogenic status, mechanical load, and preoperative osteoarthritis [21]. Particularly, the studies that used OCA transplantation in this systematic review did not report graft type or the host environment; hence, it is possible that it was used for bipolar lesions, a known predictor of failure, and could explain the high revision rate (26.9%) [21]. The high revision rate could also be attributed to potentially large lesion sizes [21].

ACI and MFx demonstrated excellent outcomes with minimal complication rates. ACI is more likely to be successful in this young population due to the younger age and low likelihood of osteoarthritic changes [23•, 24]. MFx may show great potential as a technique as it uses a minimally invasive technique to capitalize on the increased proliferative capacity of mesenchymal stem cells in adolescents for superior tissue regeneration and, thus, excellent clinical outcomes and minimal complications [20, 25]. MFx also shows superior clinical outcomes in adolescents compared to adult counterparts [20, 25]. The remaining techniques such as chondroplasty demonstrated less favorable improvement, on average, of knee outcomes, compared to the previously mentioned techniques, despite their low complication rates. This finding is not surprising given that these techniques do not focus on restoring or repairing cartilage; hence, they are less likely to improve knee function to the extent of the other techniques.

The documentation and reporting of the size of lesions was rather limited in this systematic review, thus limiting our ability to draw any definitive conclusions regarding its impact on the success of certain techniques. It should be noted, however, that the size of lesions is an important factor that should be considered. It has previously been reported that the size of lesion should be taken into account when deciding upon the most ideal treatment.

Table 2 Surgical techniques/surgical outcomes

Authors (year)	Technique used	Defect location	Defect size (SD)	Radiographic outcomes	Clinical outcomes
Niethammer et al. (2017)	Autologous chondrocyte implantation	Femoral (17) Patellar (26)	5.3 cm ² (2.5)	No significant difference was seen in Keller-Lawrence grades	In the ACI group (<i>n</i> = 67), the mean subjective IKDC score significantly increased in 100% (<i>n</i> = 40) of measured patients (<i>p</i> = 0.002) and Cincinnati Knee Rating Scale scores significantly increased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001). In the ACI group (<i>n</i> = 67), mean VAS scores significantly increased postoperatively in 100% (<i>n</i> = 67) of measured patients (<i>p</i> < 0.01). In the ACI group (<i>n</i> = 27), mean WOMAC scores significantly decreased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001). In the ACI group (<i>n</i> = 27), SF-36, MCS, and PCS significantly increased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001)
Ogura et al. (2017)	Autologous chondrocyte implantation	Lateral femoral condyle (10), medial femoral condyle (8), trochlea (6), patella (10), lateral tibial plateau (5), medial tibial plateau (1)	6.2 cm ² (2–23.4)	No significant difference was seen in Keller-Lawrence grades	In the ACI group (<i>n</i> = 67), the mean subjective IKDC score significantly increased in 100% (<i>n</i> = 40) of measured patients (<i>p</i> = 0.002) and Cincinnati Knee Rating Scale scores significantly increased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001). In the ACI group (<i>n</i> = 67), mean VAS scores significantly increased postoperatively in 100% (<i>n</i> = 67) of measured patients (<i>p</i> < 0.01). In the ACI group (<i>n</i> = 27), mean WOMAC scores significantly decreased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001). In the ACI group (<i>n</i> = 27), SF-36, MCS, and PCS significantly increased in 100% (<i>n</i> = 27) of measured patients (<i>p</i> < 0.001)
Steadman et al. (2015)	Microfracture	Patellar (10), medial femoral condyle (7), lateral femoral condyle (9)	NR	NR	In the microfracture group (<i>n</i> = 26), the mean Lysholm score and Tegner activity score significantly increased in 100% of patients (<i>n</i> = 26) (<i>p</i> < 0.05). In the microfracture group, mean patient satisfaction was 10 which had a significant correlation with Lysholm scores (<i>p</i> = 0.001)
Murphy et al. (2014)	Osteochondral allograft transplantation	Medial femoral condyle (18), lateral femoral condyle (15), patella (3), trochlea (2), tibial plateau (4), multiple (4)	NR	NR	In the OAT group (<i>n</i> = 78), mean IKDC scores significantly increased in 100% (<i>n</i> = 78) of patients (<i>p</i> < 0.05). Additionally, KS-F scores significantly increased in 100% (<i>n</i> = 78) of patients (<i>p</i> < 0.05). In 100% (<i>n</i> = 39) of measured patients, based on the modified Merle d'Aubigné-Postel scale, 87.5% of patients had a “good” or “excellent” score postoperatively. In the OAT group (<i>n</i> = 39), 100% (<i>n</i> = 39) of measured patients were noted to be “satisfied” with their knee outcome

Table 2 (continued)

Authors (year)	Technique used	Defect location	Defect size (SD)	Radiographic outcomes	Clinical outcomes
Pennock et al. (2013)	Osteochondral allograft transplantation	Femoral condyle (33)	8.4 cm ² (2.2 to 20.8)	NR	In the OAT group (<i>n</i> = 78), mean IKDC scores significantly increased in 100% (<i>n</i> = 78) of patients (<i>p</i> < 0.05). Additionally, KS-F scores significantly increased in 100% (<i>n</i> = 78) of patients (<i>p</i> < 0.05). In 100% (<i>n</i> = 39) of measured patients, based on the modified Merle d'Aubigné-Postel scale, 87.5% of patients had a "good" or "excellent" score post-operatively. In the OAT group (<i>n</i> = 39), 100% (<i>n</i> = 39) of measured patients were noted to be "satisfied" with their knee outcome
Chotel et al. (2011)	Internal fixation	NR	NR	NR	In the internal fixation group (<i>n</i> = 71), the mean subjective IKDC score significantly increased in 100% of measured patients (<i>n</i> = 37) (<i>p</i> < 0.05). Additionally, 56.7% (<i>n</i> = 21) of measured patients noted at least a "good" HSS score. In the internal fixation group (<i>n</i> = 33), 93.9% (<i>n</i> = 31) of measured patients were noted to be at least "satisfied" with their knee outcome
Schmal et al. (2010)	Internal fixation	NR	NR	The radiological outcome score did not correlate with the HSS score (85.73 ± 0.81 with abnormal radiological findings vs. 88.33 ± 1.67 with anatomical restitution)	In the internal fixation group (<i>n</i> = 71), the mean subjective IKDC score significantly increased in 100% of measured patients (<i>n</i> = 37) (<i>p</i> < 0.05). Additionally, 56.7% (<i>n</i> = 21) of measured patients noted at least a "good" HSS score. In the internal fixation group (<i>n</i> = 33), 93.9% (<i>n</i> = 31) of measured patients were noted to be at least "satisfied" with their knee outcome
Macmull et al. (2011)	Autologous chondrocyte implantation	Medial femoral condyle (15), lateral femoral condyle (7), patella (8), trochlea (3)	5.25 cm ²	NR	In the ACI group (<i>n</i> = 98), mean subjective IKDC score significantly increased in 100% (<i>n</i> = 40) of measured patients (<i>p</i> = 0.002) and Cincinnati Knee Rating Scale scores significantly increased in 100% (<i>n</i> = 57) of measured patients (<i>p</i> < 0.05)
Salzmann et al. (2012)	Microfracture	Medial femoral condyle (3), lateral femoral condyle (2), patella (2), lateral tibial plateau (1)	1.2 cm ²		In the microfracture group (<i>n</i> = 36), the mean Lysholm score and Tegner activity score significantly increased in 100% of patients (<i>n</i> = 36) (<i>p</i> < 0.05). IKDC and NAS-P scores significantly improved in 100% (<i>n</i> = 10) of measured patients
Kang et al. (2018)	Internal fixation	Medial patellar facet (14), lateral femoral condyle (11), both (4)	≤ 2 cm ² (8) > 2 cm ² (11)		In the internal fixation group (<i>n</i> = 71), mean subjective IKDC score significantly increased in 100% of measured patients (<i>n</i> = 37) (<i>p</i> < 0.05). Additionally, 56.7% (<i>n</i> = 21) of measured patients noted at least a "good" HSS score. In the internal fixation group (<i>n</i> = 33), 93.9% (<i>n</i> = 31) of measured

Table 2 (continued)

Authors (year)	Technique used	Defect location	Defect size (SD)	Radiographic outcomes	Clinical outcomes
Kang et al. (2018)	Cartilage excision	Medial patellar facet (14), lateral femoral condyle (3), both (2)	$\leq 2 \text{ cm}^2 = 14$ $> 2 \text{ cm}^2 = 10$	NR	patients were noted to be at least "satisfied" with their knee outcome In the cartilage and excision drilling group ($n = 24$), 100% ($n = 24$) of patients reported satisfactory knee outcomes
Fabricant et al. (2018)	Internal fixation			56% ($n = 5/9$) of patients demonstrated satisfactory cartilage restoration on MRI examination	In the internal fixation group ($n = 71$), the mean subjective IKDC score significantly increased in 100% of measured patients ($n = 37$) ($p < 0.05$). Additionally, 56.7% ($n = 21$) of measured patients noted at least a "good" HSS score. In the internal fixation group ($n = 33$), 93.9% ($n = 31$) of measured patients were noted to be at least "satisfied" with their knee outcome

For instance, in non-adolescent populations, it has been stated that ACI is ideally performed in patients with a lesion size of greater than 4 cm^2 ; however, techniques such as OCA transplantation may succeed irrespective of lesion size [26]. As a result, such considerations may be prognostic in determining the success of certain techniques in this sensitive population and must be considered in the future studies to ascertain appropriate guidelines [27].

The strengths of this systematic review stem from the rigorous methodology employed which includes a broad search strategy conducted on multiple databases, and a duplicate systematic approach to reviewing the literature. The systematic screening approach was employed in duplicate, thus minimizing reviewer bias. There was excellent agreement at all screening stages and for the quality assessment, thus suggesting that a thorough methodology was used throughout the preparation of this manuscript. Especially with respect to temporality, the two strengths of appropriate follow-up period and appropriate end points for assessment were critical in ensuring results were assessed appropriately despite being of such low quality of evidence.

The most significant limitations of this review are the lack of high-quality studies with large sample sizes and long-term follow-up in the literature pertaining to each technique and the methodological heterogeneity (due to inconsistency in patient characteristics, pathology, surgical techniques, length of follow-up, and outcomes). Moreover, there was a lack of reporting on skeletal maturity and type of lesions which limited the conclusions regarding its role in predicting outcomes. Finally, due to similarities in patient characteristics and etiology, it was difficult to completely exclude OCD patients who had concurrent chondral-only defects which ultimately limited the ability to make definitive conclusions pertaining to patients with purely chondral defects.

As a result, future studies with long-term follow-up, larger sample sizes, and randomized designs are needed to further confirm the results found in existing studies, especially in studies investigating the use of osteochondral autologous transplantation. Ideally, future studies will have improved documentation of necessary data (i.e., demographics, outcomes, skeletal maturity, graft failures, and complications), which is often lacking in the available literature. Future studies should also focus on indications for each technique in order to determine the best treatment for various combinations of signs and symptoms.

Conclusion

Overall, ACI was the most commonly used technique. Furthermore, ACI, MFx, OCA transplantation, and internal fixation show the most promise in treating the pediatric population due to positive postoperative functional outcomes and low complication rates. However, future studies with large sample sizes, standardized outcome documentation, and long-term follow-up are required to confirm these preliminary results.

Compliance with Ethical Standards

Conflicts of Interest Ryan P. Coughlin, MD FRCS, Amav Gupta, MD (Cand.), Olawale A. Sogbein, MD (Cand.), Ajaykumar Shanmugaraj, BHSc, Adrian Z. Kurz, MD, FRCS, Nicole Simunovic, MSc, Yi-Meng Yen, MD PhD, and Olufemi R. Ayeni, MD PhD FRCS, declare no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Appendix

Table 3 Search strategy

Embase	
1	Exp articular cartilage/ or cartilage.mp. or exp. cartilage
2	Chondr.mp. or exp. chondrpathy/
3	Exp osteochondritis/ or osteochondr*.mp. or exp. osteochondritis dissecans/
4	Exp knee/ or exp. knee injury/ or knee.mp.
5	Patella*.mp. or exp. patella/
6	Exp adolescent/ or adolescent.mp.
7	Surg*.mp.
8	1 or 2 or 3
9	4 or 5
10	6 and 7 and 8 and 9
11	Limit 10 to (human and English language)
MEDLINE ^a	
1	Exp adolescent/ or adolescent.mp.
2	Exp cartilage, articular/ or exp. cartilage/ or cartilage*.mp.
3	Exp chondrocytes/ or chondr*.mp.
4	4 exp. osteochondritis/ or osteochondr*.mp. or exp. osteochondritis dissecans
5	Exp knee/ or exp. knee joint/ or exp. knee injuries/ or knee*.mp.
6	Exp articular cartilage/ or cartilage.mp. or exp. cartilage
7	Exp patella/ or exp. patellofemoral joint/ or patella*.mp.
8	Surg*.mp.
9	2 or 3 or 4
10	5 or 6
11	1 and 7 and 8 and 9
12	Limit 10 to (human and English language)

^a Ovid MEDLINE Epub ahead of print, in-process and other non-indexed citations, Ovid MEDLINE[®] daily and Ovid MEDLINE[®] 1946 to present

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Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

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Purpose: To perform a systematic review of the use of autologous chondrocyte implantation (ACI) in the adolescent knee. **Specific aims:** (1) quantify clinical outcomes of ACI in adolescent knees, (2) identify lesion and patient factors that correlate with clinical outcome, and (3) determine the incidence of complications of ACI in adolescents. **Methods:** PubMed, MEDLINE, SCOPUS, CINAHL, and Cochrane Collaboration Library databases were searched systematically. **Outcome scores recorded included the**

- International Knee Documentation Committee score, the International Cartilage Repair Society score, the Knee Injury and Osteoarthritis Outcome score, the visual analog scale, the Bentley Functional Rating score, the Modified Cincinnati Rating System, Tegner activity Lysholm scores, and return athletics. Outcome scores were compared among studies based on the proportion of adolescents achieving specific outcome quartiles at a minimum of 1-year follow-up. The methodological quality of studies was evaluated by Coleman methodology scores (CMSs). Results:** Five studies reported on 115 subjects who underwent ACI with periosteal cover (ACI-P; 95, 83%), ACI with type I/ type III collagen cover (ACI-C; 6, 5%), or matrix-induced ACI (MACI; 14, 12%). The mean patient age was 16.2 years (range, 11 years to 21 years). All studies were case series. Follow-up ranged from 12 to 74 months (mean, 52.3 months). The mean defect size was 5.3 cm² (range, 0.96 cm² to 14 cm²). All studies reported improvement in clinical outcomes scores. Graft hypertrophy was the most common complication (7.0%). The mean preoperative clinical outcome percentage (based on the percentage of outcome scale used) was 37% (standard deviation (SD), 18.9%), and the mean postoperative clinical outcome percentage was 72.7% (SD, 16.9%). The overall percentage increase in clinical outcome scores was 35.7% (SD, 14.2%). The mean CMS was 47.8 (SD, 8.3). **Conclusions:** Cartilage repair in adolescent knees using ACI provides success across different clinical outcomes measures. The only patient- or lesion-specific factor that influenced clinical outcome was the shorter duration of preoperative symptoms. **Level of evidence:** level IV, a systemic review of level I–IV studies.
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19. Shanmugaraj A, Coughlin RP, Kuper GN, et al. Changing trends in the use of cartilage restoration techniques for the patellofemoral joint: a systematic review. *Knee Surg Sports Traumatol Arthrosc.* 2018. <https://doi.org/10.1007/s00167-018-5139-4> **Purpose:** The patellofemoral (PF) joint contains the thickest articular cartilage in the human body. Chondral lesions to this area are often misdiagnosed and can predispose to secondary osteoarthritis if left untreated. Treatment options range from arthroscopic debridement to cartilage restoration techniques such as microfracture (MFx), autologous chondrocyte implantation (ACI), and osteochondral autograft transplantation. The purpose of this study was to systematically assess the trends in surgical techniques, outcomes, and complications of cartilage restoration of the PF joint. **Methods:** This review has been conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The electronic databases PubMed, MEDLINE, and EMBASE were searched from January 1, 2007, to April 30, 2018. The Methodological Index for Nonrandomized Studies (MINORS) was used to assess study quality. A two-proportion z test was used to determine whether the differences between the proportions of cartilage restoration techniques used from 2007 to 2012 and from 2013 to 2018 were statistically significant. **Results:** Overall, 28 studies were identified, including 708 patients (824 knees) with a mean age of 39.5 ± 10.5 years and a mean follow-up of 39.1 ± 16.0 months. Majority of patients were treated with ACI (45.5%) and MFx (29.6%). A significant increase in the use of the third-generation ACI occurred with a simultaneously decreased usage of the conventional MFx over the last 5 years ($p < 0.001$). All techniques had significant ($p < 0.05$) improvements in clinical outcomes. The overall complication rate was 9.2%, of which graft hypertrophy (2.7%) was the most prevalent. **Conclusions:** ACI was the most common restoration technique. The use of third-generation ACI has increased with a concurrent decline in the use of conventional MFx over the latter half of the past decade ($p < 0.001$). Overall, the various cartilage restoration techniques reported improvements in patient-reported outcomes with low complication rates. Definitive conclusions on the optimal treatment remain elusive **due to a lack of high-quality comparative studies. Level of evidence: level IV, a systematic review of level II–IV studies.**
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22. Valtanen RS, Arshi A, Kelley BV, Fabricant PD, Jones KJ. Articular cartilage repair of the pediatric and adolescent knee with regard to minimal clinically important difference: a systematic review. *Cartilage.* 2018;194760351878350. <https://doi.org/10.1177/1947603518783503> **Objective:** To perform a systematic review of clinical outcomes following microfracture (MFx), autologous chondrocyte implantation (ACI), osteochondral allograft (OCA) transplantation, 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 of age ≤ 19 years who were treated for symptomatic knee chondral lesions with a minimum of 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 years 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 transplantation. ACI ($p < 0.001$, $p = 0.008$) and OCA transplantation ($p < 0.001$) 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:** Outcome 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.
23. 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. <https://doi.org/10.1177/1947603516630786> **Objective:** Autologous chondrocyte implantation (ACI) has not been proven to be durable over the long term. The purpose of this systematic review was (1) to evaluate activity level and knee function, (2) to evaluate reoperation and failure rates, and (3) to analyze risk factors for reoperation and failure of ACI at minimum long-term follow-up. **Design:** A comprehensive review was performed for studies with long-term outcomes after ACI for cartilage defect repair. Studies reported outcome scores such as Tegner score, Lysholm score, and International Knee Documentation Society (IKDC) score along with rates of failure and reoperation. Modified Coleman methodology scores were calculated to assess study methodological quality. **Results:** Nine studies with a total of 771 patients with a mean age of 33.4 ± 2.5 years, mean defect size of 5.9 ± 1.6 cm², and mean follow-up of

- 11.4 years were included. The Tegner score, Lysholm score, and IKDC score change from preoperative to final follow-up was 1.1 point (95% CI 0.8–1.4, $p < 0.001$), 24.9 points (95% CI 18.8–31, $p < 0.001$), and 16.5 points (95% CI 5.4–27.5, $p < 0.01$), respectively. The mean failure and reoperation rates were 18% and 37%, respectively. Increased age and lesion size ($> 4.5 \text{ cm}^2$) were significantly correlated with an increased risk of reoperation and failure. Conclusions: Overall, ACI demonstrated successful outcomes in 82% of patients over the long term. Increased patient age and lesion size greater than 4.5 cm^2 were risk factors for a higher reoperation and failure rate. Nonetheless, this review is limited by heterogeneity in surgical technique and by lesion and patient characteristics.**
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