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Microfracture produces inferior outcomes to other cartilage repair techniques in chondral injuries in the paediatric knee

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Abstract

Introduction: Chondral injuries are becoming increasingly common in the paediatric knee. First line surgical therapy is usually microfracture (MF), but the emergence of alternative techniques raises the question of what is the optimal treatment in paediatric patients.

Sources of data: A comprehensive search of PubMed, OVID, Web of Science, SportDiscus and Cochrane databases was performed using the key words 'autologous chondrocyte implantation, MF, mosaicplasty, juvenile, paediatric'.

Areas of agreement: Each technique demonstrated a significant post-surgical improvement in clinical outcome scores. However, MF demonstrated poorer outcomes in larger lesions (>3 cm^2) and shorter durability.

Area of controversy: The quality of the available literature is poor, and there is a lack of comparative trials.

Growing points: The impact of defect characteristics, mechanism of injury and concomitant surgeries should be investigated.

Areas timely for developing research: Appropriately powered randomized controlled trials with suitably long follow up and condition-specific outcome measures should compare different techniques against each other and placebo.

Key words: microfracture, cartilage repair, paediatric

Introduction

Chondral and osteochondral injuries of the knee are becoming increasingly prevalent in the paediatric population.[1] Traumatic cartilage lesions often occur concurrently with other knee pathologies, such as meniscal tear, ligament rupture and most commonly with acute lateral patellar dislocations, in which osteochondral fractures are reported in 25–75% of cases.[2] The most common cause of a non-traumatic chondral defect of the juvenile knee is osteochondritis dissecans (OCD),[3,4] a chronic condition, characterized by subchondral bone necrosis.[5] These injuries are serious, as they have the potential to progress to early osteoarthritis.[6,7]

Conservative management includes immobilization, activity modification and physiotherapy.[8] If this fails, surgical treatment is often indicated for these lesions to maintain the integrity of the knee and prevent future degeneration. For an acute osteochondral injury with a salvageable fragment, the optimal management is prompt reduction and fixation, often with metallic cannulated screws, although newer bioabsorbable devices have shown equally promising results.[3,8] Success rates between 81.8% and 94% have been reported for this technique.[8]

For lesions that are unsuitable for internal fixation, first line therapy is microfracture (MF). This technique uses an awl to stimulate the underlying subchondral bone marrow and produces a fibrin clot in the defect. The clot contains pluripotent mesenchymal stem cells that are able to differentiate into finrochondrocytes.[9,10] The resulting fibrocartilaginous repair tissue has a relatively high content of type I collagen, and hence inferior biomechanical characteristics compared with the native hyaline cartilage.[10] Second line therapies aim to restore the native hyaline cartilage over the chondral defect, and include osteochondral autograft transplantation (OAT), osteochondral allograft transplantation (OALT) and autologous chondrocyte implantation (ACI). OAT and OALT aim to fill the chondral defect with a size-matched autograft or allograft, taken from a non-weight-bearing area of the host knee or a fresh cadaver knee. ACI aims to repair a defect by filling it with cultured chondrocytes covered with a periosteal graft (P-ACI; First generation), type I/III collagen membrane (C-ACI; Second generation) or cell seeded scaffold (M-ACI; Third generation).[11] These techniques have all shown promising long-term outcomes in high quality studies of adult patients,[12–14] but are limited by high costs and technical complexity compared with MF. Furthermore, each technique has demonstrated superior results in younger patients, which reflects the fact that the healing potential of the paediatric knee is superior to adults,[4,6] with more efficient cartilage regeneration and less comorbidity.[1,15]

Although outcomes from these cartilage repair techniques have been extensively documented in the adult knee, controversy regarding the optimal treatment still exists. Furthermore, the literature on the paediatric knee is scarce. Therefore, this review aims to answer the following questions: (i) what is the quality of the current literature on surgical management of chondral defects in the paediatric knee? (ii) Which procedure has demonstrated the best clinical outcomes: MF, OAT, OALT or ACI (iii) Are there any patient- or defect-specific factors that affect surgical outcomes?

Methods

A systematic review of the literature was conducted using the following databases: PubMed, OVID, Web of Science, SportDiscus and the Cochrane Central Register of Controlled Trials. The search was performed on December 1, 2014 . Search terms included the following: ACI, matrix-assisted ACI, MF, marrow stimulation, OAT, OALT, mosaicplasty, osteochondral plugs, adolescent, children, teenage, juvenile, immature and paediatric. The Boolean operators OR and AND were used to increase the specificity of the search. Levels of evidence I–IV (according to the Oxford Centre for Evidence-Based Medicine used by the American version of the *Journal of Bone and Joint Surgery*[16]) were assessed.

The inclusion criteria were the following:

- English language.
- Human subjects.
- Level I–IV evidence.
- Evaluation of the paediatric population. We defined this as ≤21 years old for two reasons: (i) research on the expression of cartilage-specific markers in chondrocytes has determined that the

border between juvenile and adult may be up to 20 years.[17] (ii) To allow inclusion of studies reporting patients ≤21 years old. If a study contained both adult and paediatric data, the article was included if the outcomes were reported separately, so that paediatric data could be extracted.

- Reports clinical or functional outcomes from cartilage repair surgery.
- Evaluation of the knee joint only (including medial and lateral femoral condyles (LFCs), trochlea, patella and medial and lateral tibial plateaus).
- Studies that compared one procedure against another. e.g. OAT compared with MF.
- Studies involving other concomitant surgical interventions, provided they were clearly explained, and there was the only one procedure for cartilage repair.
- Results of studies with a minimum follow up of 12 months.

The exclusion criteria were the following:

- Studies not published in English.
- Reviews, case reports, expert opinion, commentary, surgical techniques, letters to the editor, basic science investigations,or animal studies.
- Studies that included adults only (>21 years), or failed to report paediatric results separately.
- Studies in which two cartilage repair procedures were performed concomitantly.
- Results of studies with a minimum follow up of <12 months.
- Evaluation of any joint other than the knee (including talus, humeral head, femoral head and acetabulum).

The initial search of all databases produced 517 results. Figure 1 shows the application of the inclusion and exclusion criteria. Removing duplicates, and applying initial search filters (English language, abstract available and human subjects) left 124 results. This number was further reduced to 30 after excluding papers based on title/abstract. Articles were regarded as relevant and warranting inclusion if they described clinical or functional outcomes from cartilage repair in the paediatric knee. Where there was uncertainty about inclusion of a study based on its title and abstract, the full article was retrieved. After strictly applying all other exclusion criteria, 13 articles were chosen for inclusion in this review.

To assess the quality of the studies we used the Coleman Methodology Score (CMS).[18,19] The CMS was initially designed for the grading of clinical studies on patellar and Achilles tendinopathy. We used a modified Coleman Methodology Score (MCMS) (Table 1) to assess the methodology of our included studies with the use of ten criteria, giving an overall score between 0 and 100 (excellent, 85–100; good, 70–84; fair, 55–69 and poor, <55), with 100 signifying a study that optimally limits chance, bias and confounders.

Results

A total of 13 studies satisfied the inclusion criteria.[1,4–6,15,20–27] Table 2 shows study demographics and patient specific data. Table 3 reports defect specific data, concomitant procedures, outcome scores and MCMS scores.

The studies comprise Level I (1), Level II (2) and Level IV (10) evidence. Eleven studies consisted of paediatric patients only. Two reported a sample of both adult and paediatric patients,[22,26] and were included in this review, as it was possible to extract the paediatric data. The mean MCMS score was 63.5 (fair quality) (Table 2). The most common methodological limitations within studies were the study design, sample size and length of follow up.

There were a total of 285 paediatric patients, but both pre- and post-operative results were only available for 273 of these patients. There were 182 male and 103 female patients in total, with a mean follow up ranging from 1 to 8.4 years. These patients underwent one of four surgical procedures: microfracture (MF; 58 patients), osteochondral autograft transplantation (OAT; 49 patients), osteochondral allograft transplantation (OALT; 56 patients) and ACI (118 patients). Within the ACI group, patients were further categorized as ACI with a periosteal graft (P-ACI; 90 patients), ACI with a collagen type I/III membrane (C-ACI; seven patients), matrix-assisted ACI (M-ACI; 18 patients) and bone marrow stem cell implantation (BMSCI; three patients). The two most common aetiologies of knee chondral injury

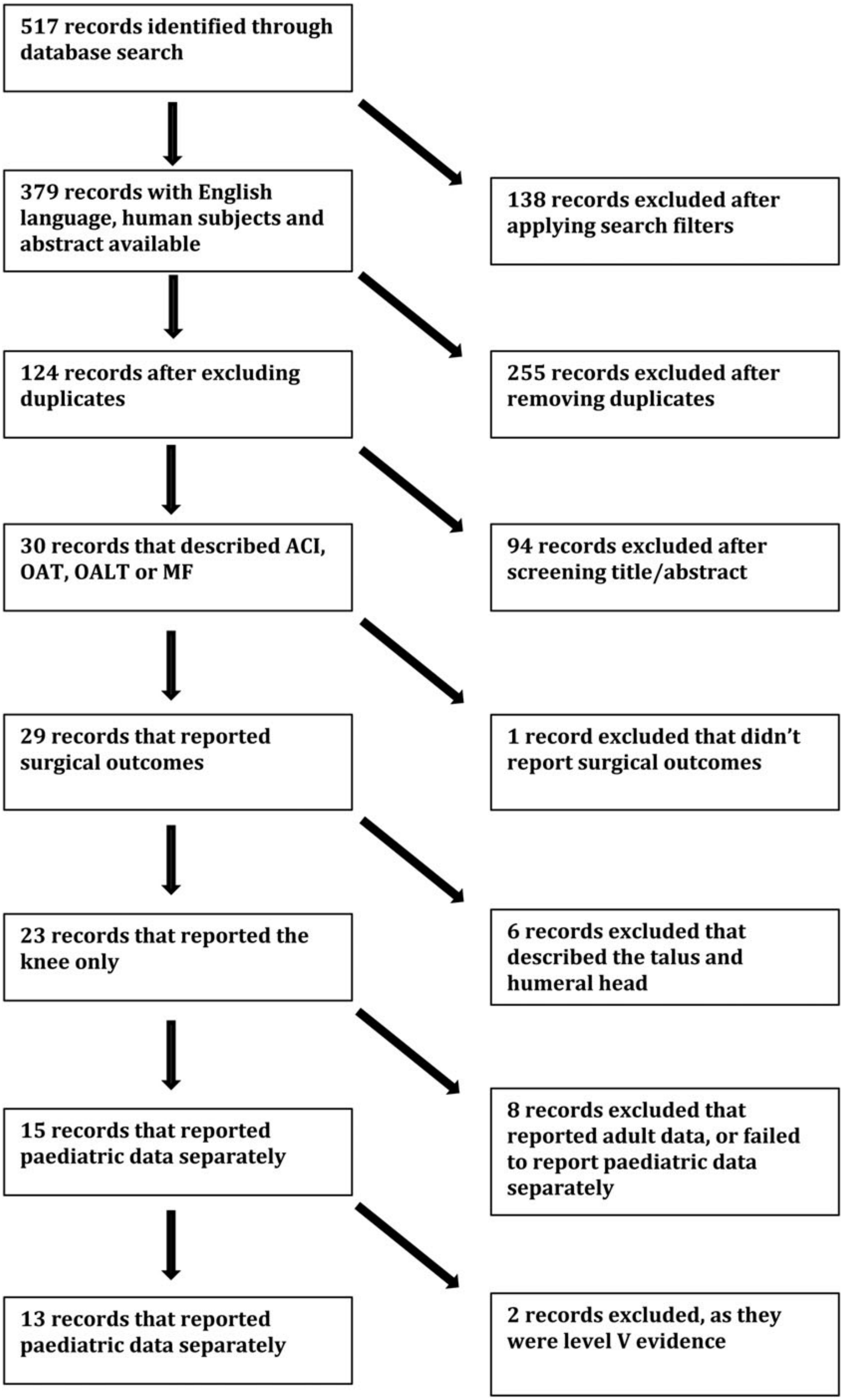

Fig. 1 Flowchart of database search; including application of inclusion/exclusion criteria.

Table 1 MCMS criteria

Criteria	Maximum score
Study size	10
Mean follow up (years)	10
Number of different cartilage repair methods (excluding procedures for concomitant injuries)	10
Study design	15
Description of surgical technique	10
Postoperative rehabilitation described?	5
Complications discussed?	10
Outcome criteria	10
Procedure of assessing outcomes	10
Description of subject selection process	10
Total	100

reported were trauma (94 lesions) and OCD (180 lesions). Other causes included chondromalacia patellae (2 lesions), degeneration (4 lesions), osteochondral fracture (2 lesions), avascular necrosis (7 lesions) and infection (1 lesion). Four patients had an unknown mechanism of injury. The mean defect size ranged from 1.2 to 7.1 cm^2 and the most common site of defect was the medial femoral condyle (MFC; 106 defects), followed by the lateral femoral condyle (LFC; 70 patients), patella (48 defects), trochlea (14 defects) and tibial plateau (4 defects). One study failed to report the mean defect size,[5] and another failed to report the location of the defects.[21]

All studies utilized subjective outcome scores. The following scores were used: IKDC (International Knee Documentation Committee; three studies),[28] ICRS (International Cartilage Repair Society; two studies),[29] Lysholm-Gillquist (four studies),[30] KOOS (Knee injury and osteoarthritis outcome score; one study),[31] modified Cincinnati knee score (two studies),[32] Tegner-Lysholm (three studies),[30] Bentley (one study), Meyer (one study), modified D'Aubigne Postel scale (two studies), NAS pain score, Hughston and VAS pain score (visual analogue scale; one study).[33]

Discussion

This systematic review assessed the quality of the current literature on cartilage repair in the paediatric knee, and specifically investigated the outcomes from MF, OAT, OALT and ACI in this patient population.

Key findings

Each article included in this review reported a significant improvement in clinical outcome scores after surgery, with the exception of Behrens *et al.*, who reported poorer outcomes after ACI at 2.6 years follow, albeit in only four patients.[26] Gudas *et al.* described a randomized controlled trial, comparing OAT against MF.[21] Both procedures demonstrated a significant improvement in outcome scores compared with pre-treatment, but only 63% of patients after MF maintained good results after 4.2 years follow up, compared with 83% after OAT. Furthermore, the MF group showed significant deterioration over the follow up period, but were still significantly improved compared with pre-surgical evaluation.

In addition to clinical outcome scores, the ability to return to pre-injury activity was mentioned in seven studies, but only quantified in four. Lyon *et al.*[15] reported that all patients returned to sports 12 months after OALT surgery, and Sasaki *et al.*[25] reported the same 6 months after OAT. Mithofer *et al.*[1] reported that 60% of patients returned to pre-injury level after ACI, whilst 96% returned to a similar high standard at 3.9 years follow up. Gudas *et al.*[21] reported that 32% of patients treated with MF achieved pre-injury activity level at 14.1 months, but only three remained at the same level after 4.2 years. The same study reported that 21 of 25 (84%) patients treated with OAT achieved the pre-injury activity level at 11.7 months, and 17 of 21 (81%) were practicing sports at the same level after 4.2 years.

The studies in this review highlighted that defect specific factors also influenced clinical outcomes, particularly in MF. Three papers reported that superior outcomes were produced by MF in lesions <3 cm^2,[6,21,24] as repeatedly documented on adult patients.[34,35] Furthermore, Salzmann *et al.*[24] reported that MF was more successful with lesions in the femoral condyles, rather than trochlear, tibial or patellar lesions. Outcomes from OAT, OALT and ACI did not show variability with lesion size or location in paediatric patients. However, Lyon *et al.*[15] stated that lesions >8 cm^2 were too large for treatment with OALT, given the difficulty in obtaining suitable allografts, and Macmull *et al.* stated that OAT

Table 2 Study and patient demographic data

Authors (Year)	Design/Evidence level	Patient demographics	Mechanism of injury	Surgical procedure	Mean follow up (Years)
P. Behrens *et al.* (2006)	Prospective clinical investigation/Level II	Number = 7 (4 with complete follow up assessments) Mean age = 18.8 M (1), F (3)	Unknown (4)	M-ACI	2.6
X.S. Dai *et al.* (2012)	Case series/Level IV	Number = 7 Mean age = 16.6 (14–19) M (5), F (2)	OCD (5) Trauma (2)	M-ACI	1
R. Gudas *et al.* (2009)	Prospective RCT/Level I	Number = 47 Mean age = 14.3 (12–18) M (28), F (19)	OCD (47)	OAT (25) MF (22)	4.2
R. Lyon *et al.* (2012)	Case series/Level IV	Number = 11 (13 lesions) Mean age = 15.2 (13–20.4) M (6), F (5)	OCD (13)	OALT (13)	2.0
S. Macmull *et al.* (2011)	Case series/Level IV	Number = 35 (31 with complete follow up assessments) Mean age = 16.3 (14–18) M (22), F (9)	OCD (11) Trauma (15) Chondromalacia patellae (2) Infection (1)	P-ACI (18) C-ACI (6) M-ACI (7)	5.5
L.J. Micheli *et al.* (2006)	Multi-centre observational prospective cohort study/Level II	Number = 37 (32 with complete follow up assessments) Mean age = 16 (11–17) M (22), F (15)	OCD (14) Trauma (29)	P-ACI	4.3
K. Mithofer *et al.* (2005)	Case series/Level IV	Number = 20 (29 total lesions in 23 knees) Mean age = 15.9 (12–18) M (15), F (5)	OCD (14) Trauma (9)	P-ACI	3.9
K. Miura *et al.* (2007)	Case series/Level IV	Number = 12 Mean age = 16.0 M (9), F (3)	OCD (12)	OAT (12)	4.5
R.T. Murphy *et al.* (2014)	Case series/Level IV	Number = 39 (43 knees) Mean age = 16.4 (11–17.9) M (26), F (17)	OCD (26) Avascular necrosis (7) Trauma (6) Other osteochondral fracture (2) Degenerative chondral lesion (2)	OALT (43)	8.4

G.M. Salzmann *et al.* (2012)	Case series/Level IV	Number = 10 Mean age = 14.1 (9–16) M (8), F (2)	OCD (3) Trauma (5) Degeneration (2)	MF	3.5
K. Sasaki *et al.* (2012)	Case series/Level IV	Number = 11 (12 knees) Mean age = 13.7 (12–16) M (9), F (2)	OCD (12)	OAT	2.2
J.R. Steadman *et al.* (2014)	Case series/Level IV	Number = 26 (28 lesions) Mean age = 16.6 (12–18.9) M (12), F (14)	Trauma (28)	MF	5.8
B.J.X. Teo *et al.* (2013)	Case series/Level IV	Number = 23 Mean age = 16.8 M (19), F (4)	OCD (23)	P-ACI (20) BMSCI (3)	6

*Abbreviations: ACI, autologous chondrocyte implantation (M = matrix, P = periosteal, C = collagen); BMSCI, bone marrow stem cell implantation; OAT, osteochondral autograft transplantation; OALT, osteochondral allograft transplantation; MF, microfracture.

was unsuitable for larger lesions because of donor site morbidity.[6]

Biopsy assessment was undertaken in 2 of 13 articles included in the present systematic review. Macmull *et al.*[6] demonstrated that 12 patients (50%) formed fibrocartilage at the graft site one year after ACI. In the adult literature, instead, biopsy assessment showed a majority of hyaline cartilage formation after ACI in most instances.[14] Gudas *et al.*[21] biopsied 11 OAT patients, and reported that they all demonstrated hyaline cartilage repair tissue one year postoperatively, whereas the 14 MF patients in the same study demonstrated inferior fibrocartilage repair tissue.

Strengths and limitations

The major strength of this systematic review is that it is the first of its kind on cartilage repair procedures in the paediatric knee. Therefore, orthopaedic surgeons can use it to guide their decision making when treating paediatric patients.

This review included a comprehensive search of five major databases, with broad inclusion and exclusion criteria that were specific to its purpose. One study included was level I evidence,[21] two studies were Level II evidence,[4,26] and three studies had an MCMS>70 (good quality).[1,6,21] The mean follow up across all studies was 4.15 years, with only one reporting follow up <2 years.

The quality of the evidence included in this review is an important limitation to the findings. Two articles were graded as poor (MCMS<55),[24,26] and seven as fair (MCMS<69).[4,5,15,20,22,25,27] Furthermore, there was only one RCT,[21] and the two Level II studies were graded as fair and poor respectively.[4,26] Only one article reported a comparative trial of two different techniques.[21] Another limitation is the absence of a control group across all studies, and the large number of potential confounders, such as patient demographics, defect characteristics, mechanism of injury and concomitant or previous surgeries.

Some of the outcome measures used in the studies may also face validity criticism. Only the KOOS, IKDC, ICRS and Lysholm-Gillquist scores have been validated for knee cartilage lesions.[28–31,36] Three studies failed to include any of these scores,[4,6,22]

Table 3 Defect specific data, concomitant procedures, outcomes and MCMS

Authors (Year)	Defect size /location	Concomitant procedures	Clinical outcome scores	MCMS
P. Behrens *et al.* (2005)	Mean defect size = 4.35 cm^2 MFC (1) LFC (2) Patella (1)	Unknown	Meyer, Tegner, Lysholm, ICRS	48
X.S. Dai *et al.* (2012)	Mean defect size = 7.1 cm^2 (4–12) MFC (4) LFC (2) MFC/trochlea (1)	Meniscal repair (1), Subchondral bone grafting (2)	IKDC, ICRS, Lysholm, KOOS	60
R. Gudas *et al.* (2009)	Mean defect size = 3.20 cm^2 (OAT), 3.17 cm^2 (MF)	Unknown	ICRS, Tegner	96
R. Lyon *et al.* (2012)	Mean defect size = 5.1 cm^2 MFC (4) LFC (7) Patella (1) Trochlea (1)	Unknown	Modified D'Aubigne-Postel scale	59
S. Macmull *et al.* (2011)	Mean defect size = 5.26 cm^2 (0.96–15.8) MFC (14) Patella (7) LFC (6) Trochlea (3)	Malalignment (1) Bone deficiency correction (2)	VAS, Bentley, modified Cincinnati	72
L.J. Micheli *et al.* (2006)	35 single defects, mean size = 5.4 cm^2 2 multiple defects, mean total defect size = 2.8 cm^2 MFC (22) LFC (15)	Debridement (30) Fragment reattachment/ removal (14) Meniscal repair (6) Patellar realignment (5) Ligament repair (3) Internal fixation of OCD lesion (2)	Modified Cincinnati	59
K. Mithofer *et al.* (2005)	Mean defect size = 6.4 cm^2 MFC (14) LFC (6) Trochlea (4) Tibial plateau (2) Patella (1)	Autologous bone grafting (2) ACL reconstruction (2) Meniscal repair (4) Tibial tubercle osteotomy (1)	Lysholm, Tegner	70
K. Miura *et al.* (2007)	Mean defect size = 2.4 cm^2 MFC (10) LFC (2)	Patellofemoral realignment (1) Lateral discoid meniscentomy (1)	Hughston rating scale	64
R.T. Murphy *et al.* (2014)	Mean graft size = 8.4 cm^2 MFC (18) LFC (15) Patella (3) Trochlea (2) Tibial plateau (1) Multiple sites (4)	Epiphysiodesis (1) High tibial osteotomy (1) Tibial tubercle osteotomy (1) Hardware removal (2) MF/drilling MFC (3) Loose body removal (3) Proximal patellofemoral realignment (3) Repair of lateral meniscus (1)	Merle d'Aubigne-Postel scale, IKDC, Knee Society function score	71

Table continues

Table 3 Continued

Authors (Year)	Defect size /location	Concomitant procedures	Clinical outcome scores	MCMS
G.M. Salzmann *et al.* (2012)	Mean defect size = 1.2 cm^2 MFC (3) LFC (2) Trochlea (2) Patella (2) Tibial plateau (1)	Unknown	IKDC, Lysholm, Tegner NAS	40
K. Sasaki *et al.* (2012)	Mean defect size = 2.7 cm^2 MFC (8) LFC (4)	Unknown	IKDC, Lysholm	64
J.R. Steadman *et al.* (2014)	Mean defect size = 1.77 cm^2 (MFC), 1.88 cm^2 (LFC), 2.09 cm^2 (patella) MFC (8) LFC (9) Patella (10) Trochlea (1)	ACL reconstruction (6) Other ACL repair (4) Partial meniscectomy (3) Meniscus repair (3)	Lysholm, Tegner,	62
B.J.X. Teo *et al.* (2012)	Patella (23)	Realignment procedures in some patients due to patellar instability (number not specified)	IKDC, Lysholm, Tegner	60

which may limit the validity of their findings, although all outcome scores reported were validated for other knee pathologies.[37] The Cincinnati and Tegner activity scores are validated for other knee injuries, and the D'Aubigne Postel scale, which was used in two studies, has not been validated for the knee.[15]

The studies in this review also lacked a long-term assessment of patients into adulthood, with a mean follow up of 4.15 years. Therefore, we cannot comment on the long-term durability and survivorship of the repaired cartilage defects, and determine whether there is a reduced risk of subsequent osteoarthritis, or a requirement for joint reconstruction in the long-term. Finally, articles published in languages other than English and unpublished materials were not included in this review, which may have resulted in a language selection bias.

Future directions

There is an urgent need for more high quality studies on the management of articular cartilage injury in young patients, including large prospective, randomized controlled trials, with very strict patient criteria regarding site, size and aetiology of lesion and comparisons between different repair techniques, or with a placebo group. These studies should also control for potential confounders such as preoperative duration of symptoms, past surgical history and concomitant procedures. Finally, there should be a control group similar to the intervention group in all features other than the intervention performed.

Conclusion

This systematic review shows that MF, OALT, OAT and ACI have all been implemented successfully in the paediatric knee. However, MF was generally associated with poorer outcomes, and shorter durability than the other techniques, particularly in larger lesions (>3 cm^2). The superiority of the other techniques was attributed to the more anatomical hyaline cartilage repair tissue they formed, compared with the less durable fibrocartilage tissue produced after MF. Whilst MF is technically the simplest procedure, its selection as first line therapy for chondral lesions in the paediatric knee can be questioned. This review could not however answer the question of which alternative technique should be preferred, given the general low quality of the literature and lack of comparative trials. Only further prospective RCTs will elucidate the optimal surgical treatment for focal chondral injury in the paediatric knee.

References

1. Mithöfer K, Minas T, Peterson L, et al. Functional outcome of knee articular cartilage repair in adolescent athletes. *Am J Sports Med* 2005;33:1147–53.
2. Kramer DE, Pace JL. Acute traumatic and sports-related osteochondral injury of the pediatric knee. *Orthop Clin North Am* 2012;43:227–36.
3. Macmull S, Skinner JA, Bentley G, et al. Treating articular cartilage injuries of the knee in young people. *BMJ* [Online] 2010;340:c998. Available from: doi: 10.1136/bmj.c998. Available from: http://www.bmj.com/content/340/bmj.c998.
4. Micheli LJ, Moseley JB, Anderson AF, et al. Articular cartilage defects of the distal femur in children and adolescents: treatment with autologous chondrocyte implantation. *J Pediatr Orthop* 2006;26:455–60.
5. Teo BJX, Buhary K, Tai B, et al. Cell-based therapy improves function in adolescents and young adults with patellar osteochondritis dissecans. *Clin Orthop Relat Res* 2013;471:1152–8.
6. Macmull S, Parratt MT, Bentley G, et al. Autologous chondrocyte implantation in the adolescent knee. *Am J Sports Med* 2011;39:1723–30.
7. Radin EL, Rose RM. Role of subchondral bone in the initiation and progression of cartilage damage. *Clin Orthop Relat Res* 1986;213:34–40.
8. Kocher MS, Czarnecki JJ, Andersen JS, et al. Internal fixation of juvenile osteochondritis dissecans lesions of the knee. *Am J Sports Med* 2007;35:712–8.
9. Camp CL, Stuart MJ, Krych AJ. Current concepts of articular cartilage restoration techniques in the knee. *Sports Health* 2014;6:265–73.
10. Gill TJ, Asnis PD, Berkson EM. The treatment of articular cartilage defects using the microfracture technique. *J Orthop Sports Phys Ther* 2006;36:728–38.
11. Goyal D, Goyal A, Keyhani S, et al. Evidence-based status of second- and third-generation autologous chondrocyte implantation over first generation: a systematic review of level I and II studies. *Arthroscopy* 2013;29:1872–8.
12. Minas T. Autologous chondrocyte implantation for focal chondral defects of the knee. *Clin Orthop Relat Res* 2001;(391 Suppl):S349–61.
13. Brittberg M, Lindahl A, Nilsson A, et al. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med* 1994;331:889–95.
14. Peterson L, Minas T, Brittberg M, et al. Two- to 9-year outcome after autologous chondrocyte transplantation of the knee. *Clin Orthop Relat Res* 2000;374:212–34.
15. Lyon R, Nissen C, Liu XC, et al. Can fresh osteochondral allografts restore function in juveniles with osteochondritis dissecans of the knee? *Clin Orthop Relat Res* 2013; 471:1166–73.
16. Obremskey WT, Pappas N, Attallah-Wasif E, et al. Level of evidence in orthopaedic journals. *J Bone Joint Surg Am* 2005;87:2632–8.
17. Schmal H, Pestka JM, Salzmann G, et al. Autologous chondrocyte implantation in children and adolescents. *Knee Surg Sports Traumatol Arthrosc* 2013;21:671–7.
18. Coleman BD, Khan KM, Maffulli N, et al. Studies of surgical outcome after patellar tendinopathy: clinical significance of methodological deficiencies and guidelines for future studies. Victorian Institute of Sport Tendon Study Group. *Scand J Med Sci Sports* 2000;10: 2–11.
19. Tallon C, Coleman BD, Khan KM, et al. Outcome of surgery for chronic Achilles tendinopathy. A critical review. *Am J Sports Med* 2001;29:315–20.
20. Dai XS, Cai YZ. Matrix-induced autologous chondrocyte implantation addressing focal chondral defect in adolescent knee. *Chin Med J* 2012;125:4130–3.
21. Gudas R, Simonaityte R, Cekanauskas E, et al. 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;29:741–8.
22. Miura K, Ishibashi Y, Tsuda E, et al. Results of arthroscopic fixation of osteochondritis dissecans lesion of the knee with cylindrical autogenous osteochondral plugs. *Am J Sports Med* 2007;35:216–22.
23. Murphy RT, Pennock AT, Bugbee WD. Osteochondral allograft transplantation of the knee in the pediatric and adolescent population. *Am J Sports Med* 2014;42:635–40.
24. Salzmann GM, Sah BR, Schmal H, et al. Microfracture for treatment of knee cartilage defects in children and adolescents. *Pediatr Rep* 2012;4:e21.
25. Sasaki K, Matsumoto T, Matsushita T, et al. Osteochondral autograft transplantation for juvenile osteochondritis dissecans of the knee: a series of twelve cases. *Int Orthop* 2012;36:2243–8.
26. Behrens P, Bitter T, Kurz B, et al. Matrix-associated autologous chondrocyte transplantation/implantation (MACT/MACI)—5-year follow-up. *Knee* 2006;13:194–202.
27. Steadman JR, Briggs KK, Matheny LM, et al. Outcomes following microfracture of full-thickness articular cartilage

lesions of the knee in adolescent patients. *J Knee Surg* 2014;28:145–50.

28. Crawford K, Briggs KK, Rodkey WG, et al. Reliability, validity, and responsiveness of the IKDC score for meniscus injuries of the knee. *Arthroscopy* 2007;23:839–44.
29. van den Borne MP, Raijmakers NJ, Vanlauwe J, et al. International Cartilage Repair Society (ICRS) and Oswestry macroscopic cartilage evaluation scores validated for use in Autologous Chondrocyte Implantation (ACI) and microfracture. *Osteoarthritis Cartilage* 2007; 15:1397–402.
30. Briggs KK, Kocher MS, Rodkey WG, et al. Reliability, validity, and responsiveness of the Lysholm knee score and Tegner activity scale for patients with meniscal injury of the knee. *J Bone Joint Surg Am* 2006;88:698–705.
31. Bekkers JE, de Windt TS, Raijmakers NJ, et al. Validation of the Knee Injury and Osteoarthritis Outcome Score (KOOS) for the treatment of focal cartilage lesions. *Osteoarthritis Cartilage* 2009;17:1434–9.
32. Barber-Westin SD, Noyes FR, McCloskey JW. Rigorous statistical reliability, validity, and responsiveness testing of the Cincinnati knee rating system in 350 subjects with uninjured, injured, or anterior cruciate ligament-reconstructed knees. *Am J Sports Med* 1999;27: 402–16.
33. Hoher J, Munster A, Klein J, et al. Validation and application of a subjective knee questionnaire. *Knee Surg Sports Traumatol Arthrosc* 1995;3:26–33.
34. Kreuz PC, Steinwachs MR, Erggelet C, et al. Results after microfracture of full-thickness chondral defects in different compartments in the knee. *Osteoarthritis Cartilage* 2006;14:1119–25.
35. Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. *J Bone Joint Surg Am* 2004;86-A:455–64.
36. Wang D, Jones MH, Khair MM, et al. Patient-reported outcome measures for the knee. *J Knee Surgery* 2010;23: 137–51.
37. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res* 1985;198: 43–9.