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Systematic review

Size of cartilage defects and the need for repair: a systematic review[☆]



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ABSTRACT

Background: Cartilage defects are treated with a wide array of non-operative and surgical procedures. Optimal choice of treatment depends on lesion depth and size.

Objectives: To review and summarize current data on the management of cartilage injuries in joints as it relates to defect size.

Data sources: MEDLINE, Cochrane Central Register of Controlled Trials & Cochrane Library, CINHAL.

Study eligibility criteria, participants, and interventions: Inclusion: (1) Studies investigating patients who underwent cartilage repair of the shoulder, elbow, hip, knee, and ankle. (2) Studies reporting outcome measures and treated lesion size. Exclusion: (1) No mention of defect size. (2) Joints not mentioned above. (3) <12 months clinical follow-up. (4) Unavailable full English or full texts.

Study appraisal and synthesis methods: Selection procedure and homogeneity of patient population and preoperative and postoperative care were examined. Attrition bias was scored based on the percentage follow-up of the primary outcome parameter. Level of evidence was determined according to the guidelines of the Oxford Center for Evidence-Based Medicine.

Results: Small lesions sized 1.5 cm² are often either fixated or conservatively treated, lesions sized >1.5 cm² mostly addressed with cell-based therapies such as autologous cartilage implantation (ACI), or matrix associated cartilage implantation (MACI). Large lesions often are the domain of osteochondral autograft transfer system (OATS).

Limitations: Prospective randomized controlled studies are not available for every joint and many studies represent case studies with limited implications for treatment decisions.

Conclusions and implications of key findings: Evidence-based treatment selection based on cartilage defect size can be beneficial.

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Introduction

Cartilage lesions in large joints are common and can occur in isolation or in combination with bone deficiencies, ligament injuries, limb malalignment, and traumatic, concomitant injuries. Each of these potential pathologies must be addressed to achieve a successful

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outcome for any cartilage restoration procedure. Focal cartilage defects result in disability that can be similar to osteoarthritis (OA).¹ The size of the lesions is a determining factor in every algorithm of decision making in terms of treatment.² The decision if a cartilage lesion demands surgical treatment is depending on a variety of parameters and should always be reached mutually between physician and patient after thorough education about risks and benefits of operative and conservative treatment options. Radiographs are often unrevealing in patients with acute joint pain after a cartilage injury. Indirect signs, such as an effusion or a loose body may be noted, but magnetic resonance imaging (MRI) is the preferred imaging modality to evaluate the depth, size, and location of cartilage lesions and subchondral bone involvement. With the broad availability of high resolution, multiplanar imaging, the diagnosis and treatment of cartilage pathologies have improved. Chondropathologies can be identified earlier in their natural progression, increasing opportunities for treatment and preservation prior to onset of degenerative changes.³

Lesion classification is of high clinical importance in determining the right treatment option. While the Outerbridge Classification, published in 1961, takes the lesion size into consideration (Grade 2: partial thickness lesions (1.5 cm in diameter; Grade 3: lesions >1.5 cm in diameter or full thickness), the widely used International Cartilage Repair Society Classification (ICRSC) combines size and depth to better characterize and describe defects.⁴ The term cartilage lesion used in this article refers to both, solitary chondral lesions (ICRS grade 1-3) and chondral lesions with affection of the subchondral bone (ICRS grade 4).

Joint preservation is the preferred treatment strategy for chondropathologies of the large joints in young and active patients in order to improve pain, restore activity, and prevent the progression of degenerative changes. Given the relatively recent emergence of the field, so far, there remains a paucity of research regarding available treatment data and results as they relate to cartilage defect size. Apart from the knee, only limited high-quality data is available to provide guidance in treatment decisions for other joints.

In this review, we focus on the primary surgical treatment options for small cartilage defects defined as those less than 1.5 to 3 cm,² depending on the joint affected. Additionally, we describe the upper limit of defect sizes that are treatable with reconstructive techniques.

Objectives

The purpose of this review is to assess and review available evidence for cartilage repair depending on the size of the lesion and thus help inform patients and surgeons about treatment strategies in this evolving field. We aim to illustrate the lower limit of defect sizes that need to be repaired in order to maintain joint integrity as well as the upper limit of lesion sizes that can and should be surgically addressed with today's available joint preservation procedures.

Material and methods

Literature search

A comprehensive literature search was conducted on May 25, 2021 following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). Queried databases included MEDLINE, the Cochrane Central Register of Controlled Trials & Cochrane Library, and CINHAL (Cumulative Index for Nursing and Allied Health Literature). No date search period parameters were set, and a Boolean algebra search strategy was utilized as follows: (Cartilage OR chondral) AND (Defect OR lesion) AND (size) AND (Shoulder OR elbow OR hip OR knee OR ankle). Articles were catalogued using Microsoft Excel (Version 16.50; 2021; Microsoft Corp). Duplicate articles, systematic reviews, in vitro studies, and non-English articles were eliminated. Abstracts of these studies were then manually reviewed by 1 author and studies not related to the research topic were removed from the list. Full texts were then retrieved and manually reviewed for inclusion. In addition, reference lists and prior studies for reviewed studies were also reviewed for any potential missed inclusions.

Inclusion criteria

- (1) Studies investigating patients who underwent cartilage repair of the shoulder, elbow, hip, knee, and ankle.
- (2) Studies reporting outcome measures and treated lesion size.

Exclusion criteria

- (1) Studies reporting on cartilage repair without mention of the treated defect size.
- (2) Studies reporting on cartilage repair of other joints than those mentioned above.
- (3) Studies reporting with less than 12 months of clinical follow-up.
- (4) Studies with unavailable full English texts.
- (5) Studies with unavailable full texts.

Seventy-four studies were identified and analyzed according to the above criteria (Fig. 1). Articles were reviewed by the senior authors until a consensus was reached regarding inclusion.

To determine the possibility of bias, we examined the selection procedure (selection bias) and homogeneity of the patient population and preoperative and postoperative care (performance bias). Attrition bias was scored based on the percentage follow-up of the primary outcome parameter. Possible detection bias was quantified by blinding of observers, validity of outcome measures, and

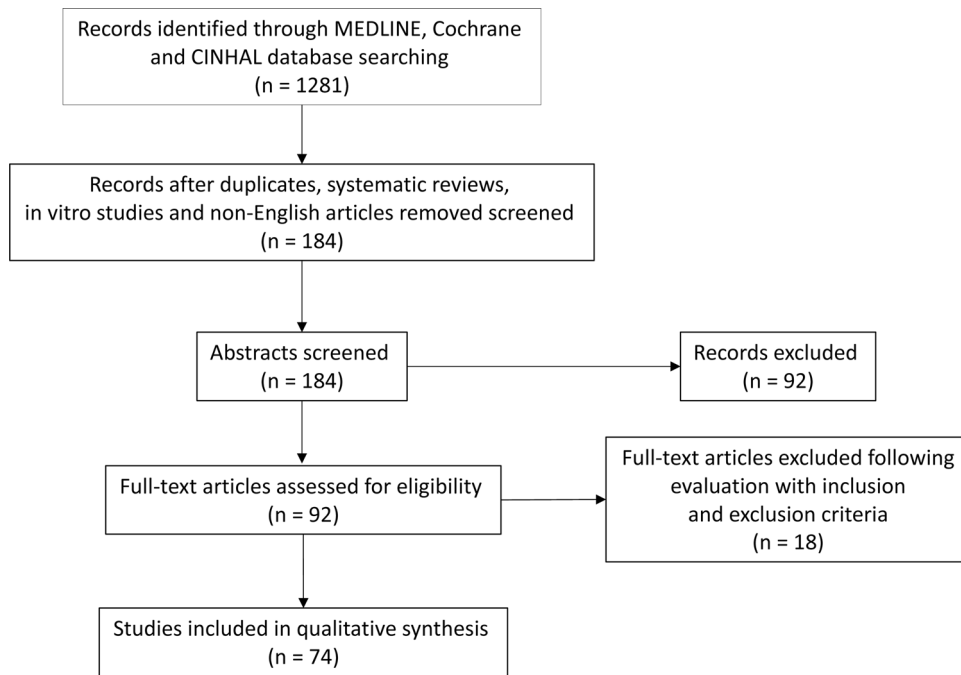


Fig. 1. Flowchart outlining the systematic review.

the statistical analysis, whereas reporting bias was assessed by differences in description of outcome parameters between the study groups. Level of evidence (LOE) was determined according to the guidelines of the Oxford Center for Evidence-Based Medicine. After this evaluation, articles were selected based on the risk of bias, modified Coleman score, on PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and LOE to answer our clinical research question.

Data were collected from articles meeting inclusion and exclusion criteria. Subsequently extracted data included authors, year of publication, journal of publication, surgical procedures analyzed, number of patients, mean age, gender, main inclusion criteria, defect location, defect size, and defect grade. Primary and secondary outcomes as well as follow-up information were recorded on standardized forms for this systematic review.

Assessment of level of evidence

Two independent reviewers evaluated each study and created a classification based on the level of evidence (LOE) using previously published criteria.⁵

Assessment of quality of evidence

The quality of evidence of the included studies was assessed using the Modified Coleman Methodology Score (MCMS) (Table X). The Coleman Methodology Score was initially described to evaluate the quality of studies investigating the treatment of tendinopathy.⁶ This score includes part A (primarily evaluates baseline study characteristics; 0-60) and part B (primarily evaluates outcome criteria and recruitment rates; 0-40) and was subsequently modified by Jakobsen et al for the assessment of cartilage repair.⁷

Two independent reviewers determined the MCMS for each study. If any discrepancy existed, all available data was reviewed, and a consensus was reached. Excellent studies scored 85 to 100, good studies scored 70 to 84, fair studies scored 55 to 69, and poor studies scored less than 55.⁷

Results

After a full-text review,⁷⁴ studies were identified for inclusion in the current study (Fig. 1).

Level of evidence

There were 12 studies of LOE 1, 11 studies LOE 2, 10 studies of LOE 3, 30 studies of LOE 4 and 7 studies of LOE 5. Although 1 study was described as LOE 1 in the published journal, this article was reassigned as LOE 2 in the current study based on the previously published criteria.⁸

Quality of evidence

The mean MCMS of the overall population of the studies was 63.4 ± 19.6 of 100 points. The mean MCMS in part A and part B were 39.3 ± 11.1 and 24.1 ± 11.0 , respectively.

Shoulder

The shoulder joint's function relies primarily on soft tissue structures to provide well-balanced and centered movement about the central axis of the joint. As long as the joint is centered, smaller cartilage defects are relatively asymptomatic, as the shoulder is subjected to relatively modest point-loading demands. In comparison, substantially higher forces are distributed throughout large portions of the joint surface of the hip, knee, and ankle.⁹ Isolated, full-thickness chondral lesions of the glenohumeral joint are a clinically significant pathology encountered by laborers, athletes, and the elderly as they tend to enlarge over time.¹⁰ While the incidence of such lesions is 5% to 17% and therefore much lower than in the hip and knee, the natural history of full-thickness chondral lesions in the shoulder is less clearly described than those of the knee or ankle.¹¹ The glenohumeral joint cartilage is relatively thin, not exceeding more than 2 mm at the central articulating surface of the humerus and becoming thinner towards the joint periphery.¹²

Siebold et al adopted the microfracture technique established in the knee and performed it on 5 patients with Outerbridge grade IV lesions of the humeral head with a mean size of 3.11 cm^2 .¹³ They reported favorable clinical and radiologic results at a mean of 26 months follow-up. Three patients underwent a second look arthroscopy and demonstrated a size reduction of the cartilage defect. Of note, 2 other patients did show signs of joint degeneration on radiographs at final follow-up.

Millett et al performed microfracture for symptomatic full-thickness cartilage defects of the glenohumeral joint in 30 patients with a mean lesion size of 3.07 cm^2 and a range of 1 to 14 cm^2 .¹⁴ Here, 24 patients reported significant improvements in patient-reported outcome scores at a mean follow-up of 47 months. While 6 patients progressed to further surgery, a negative correlation between the size of cartilage defect and ASES score was observed. This finding supports the use of microfracture in small-sized lesions.¹⁵

Another non-randomized, non-controlled trial was published by Frank et al who reported of 16 patients who underwent arthroscopic microfracturing of the humeral head and/or the glenoid surface.¹¹ The average diameter of the chondral lesions treated was $19.7 \pm 4.9 \text{ mm}$ (range, 10-25) overall, $20.8 \pm 2.9 \text{ mm}$ (range, 15-25) humeral, and $16.3 \pm 3.7 \text{ mm}$ (range, 10-20) on the glenoid. At a mean follow-up time of 28 months, a significant decrease in pain after surgery and a significant improvement in clinical outcomes were reported. 3 patients did go on to have further surgery during follow-up.

While there is no published defect size limit for microfracture in the shoulder, as is quoted consistently through the knee literature, microfracture in the shoulder is generally indicated for smaller sized lesions up to a size of 2 cm^2 , while mid-sized defects of the humeral head can be addressed with Autologous Chondrocyte Implantation (ACI).^{14,16} ACI comprises a 2-step procedure: Chondrocytes are biopsied from a donor joint surface, expanded, and applied underneath a periosteal patch (ACI) or applied and implanted on a membrane (MACI; matrix-induced autologous chondrocyte implantation). Boehm et al recently reported on 7 patients who underwent ACI for symptomatic focal grade IV cartilage lesions of the humeral head with a median size of 3 cm^2 (range $2.3\text{--}4.5 \text{ cm}^2$). At mean follow-up time of 32 months, the subjective shoulder value improved to 95% compared to 60% preoperatively.¹⁶ Postoperative median Constant score and ASES were 95-97 points, respectively. However, the authors concluded that the procedure is, in consideration of its 2-stage surgical design and the cost intensiveness, restricted to young and active patients in their practice. As of today, the procedure is only approved for use in the knee by the US Federal Drug Administration (FDA) and European Medicines Agency. Another treatment option, particularly for large defects, is osteochondral allograft transplantation (OCA). Camp et al reported a transplantation of a tibial osteochondral allograft to restore a large glenoid osteochondral defect that resulted in a significant improvement in both, QuickDASH and ASES score at 12 months follow-up.¹⁷

Kircher et al reported 9 years results of osteochondral autologous transplantation for the treatment of full-thickness cartilage defects of the shoulder.¹⁸ The mean defect size treated was relatively small with 1.5 cm^2 and it was a mean of 1.86 osteochondral cylinders used. 100% of the patients were subjectively very satisfied. No reoperations were reported, and the Mean Constant score improved from 76.2 to 90.9.

While randomized controlled trials are lacking, the available literature suggests that lesions of the glenoid and humerus 1.5 cm^2 and greater can successfully be addressed with cartilage repair and short- to midterm improvement in pain function can be expected. In general, evidence is limited and the use of cartilage repair techniques in the shoulder lacks standardization regarding location and size of the defect, resulting in variable indications for similar defects. Table 1 summarizes the available evidence.

Elbow

Most cartilage injuries of the capitellum are found in the context of osteochondritis dissecans (OCD). While first coined by Koenig in 1888, the specific pathophysiological mechanism for the development of OCD remains unclear.¹⁹ A multi-factorial etiology consisting of repetitive microtrauma, localized ischemia, genetic predisposition, and altered biomechanics is currently thought to cause this disease process.²⁰ In young patients with open physes, around 95% of the lesions may heal without surgical intervention.²¹ This number is decreased to 50% in patients with closed physes. Indications for surgery include (1) failure of conservative management, (2) unstable lesions, (3) presence of mechanical symptoms and/or loose bodies, and (4) pain in the context of daily activities. While small lesions can often undergo internal fixation with historically good outcomes, larger lesion sizes of greater than 10 to 12 mm in diameter or 50% of the capitellar articular surface are commonly treated with restorative procedures such as osteochondral autograft

Table 1
Shoulder.

Study	Journal	Year	Level	Enrolled participants	Lesion size (cm ²)	Age (years)	Treatment	Outcome parameter	Follow-up time (months)	Results
Siebold et al	Knee Surg Sports Traumatol Arthrosc	2003	IV	5	3.11	32	Mfx + periosteal flap	MRI; X-rays; Constant score; Second look arthroscopy	25.8	CS improved significantly; MRI: layer of regeneration tissue; Arthroscopy: Significant reduction of cartilage lesion
Millett et al	Arthroscopy	2009	IV	30	3.07	45.5	Mfx	ASES; Patient satisfaction	45	Significant improvement in ASES; High patient satisfaction
Frank et al	Am J Sports Med	2010	IV	16	5.07	37	Mfx	SST; ASES; VAS	27.8	Significant improvements in SST and ASES; Decrease in VAS
Buchmann et al	J Shoulder Elbow Surg	2012	IV	4	4	29.3	ACI	VAS; ASES; MRI; CS	41.3	Significant improvements in SST and ASES; Decrease in VAS; MRI with satisfactory defect coverage with signs of fibrocartilaginous repair tissue
Camp et al	Orthopedics	2015	V	1	6	25	OCA	SSV; ASES; QuickDASH	12	Significant improvement in ASES and SSV; Improved ROM
Boehm et al	J Shoulder Elbow Surg	2020	IV	7	3	42.8	ACI	SSV; ASES	32	Significant improvement in ASES and SSV

Abbreviations: ACI, autologous chondrocyte implantation; ADL, activities of daily living; ASES, American shoulder and elbow surgeons; MRI, Magnetic resonance imaging; OA, osteochondral allograft; OATS, osteochondral autograft transplantation system; OCA, osteochondral allograft transplantation; ROM, range of motion; SST, simple shoulder test; SSV, subjective shoulder value; VAS, visual analog scale.

transfer (OAT) or osteochondral allograft transplantation.^{20,22} Stage II and III lesions with a diameter of up to 10 mm and an intact lateral pillar can be treated with microfracture. Lewine et al reported on 21 patients who underwent microfracture for such lesions. While there were no revisions, 85.7% of patients returned to any sport, whereas 66.7% returned to their primary sport at the mean time of follow-up of 2.3 years. Range of motion and Timmerman scores improved significantly.²³ Regarding larger lesions, Iwasaki et al reported on 19 baseball players who underwent OATs for defects averaging 1.47 cm² at a mean follow-up of 45 months and found statistically significant improvements in Timmerman and Andrews (T&A) scores, elbow motion, pain relief (95% of patients), and a 90% return to play rate, indicating that the repair of small lesions can result in substantial clinical benefits.²⁴ While OATs has demonstrated encouraging short- and mid-term results, some patients and parents may have reservations towards a harvesting procedure on a healthy, asymptomatic knee or other donor site. Given this, OCA may provide an attractive alternative as grafts can be obtained from cadaveric femoral condyles or capitella, albeit with increased associated graft costs. Early results of OCA use in the elbow have been promising.²⁵ Mirzayan et al reported results of the treatment of 9 male baseball players with OCD of the capitellum, that were treated with an average plug diameter of 11 mm. At a mean follow-up of 48 months, Mayo Elbow Performance score improved from an average of 57.8 preoperatively to 98.9.²⁵

In summary, cartilage repair and restoration techniques of the elbow include microfracture, OATs, OCA, and ACI.^{26, 27} Microfracture is often indicated in patients with ICRS stage II and III and a lesion with a diameter of up to 10 mm²⁰. Lesions sized greater than 10 to 12 mm in diameter are usually addressed with restorative procedures such as OAT or OCA.²⁸ In the case of deficient or necrotic subchondral bone or large subchondral cysts, even small lesions are treated with structural reconstructive techniques (OATs and OCA), as reparative procedures are incapable of rebuilding the supportive bone stock necessary to support a stable cartilage bed.²⁹ An overview of current evidence in the elbow is summarized in Table 2.

Hip

The hip joint is a ball and socket synovial joint and similar to the big lower extremity joints, a major weight-bearing joint, only secondary to the knee, and amongst the largest bony articulations in the body. It plays a central biomechanical role in locomotion, while transferring the weight of the body from the axial skeleton into the lower extremities, placing high stress on the articulating cartilage surfaces of the main load carrying areas of the femoral head and the acetabulum. Even small chondral or subchondral pathologies can lead to potentially symptomatic cartilage damage, that can initiate the development of OA.³⁰ Hip related pain is a common cause for presentation in orthopedic clinics, with an estimated annual incidence of 440 per 100,000 people in the general population aged 15 to 60 years.³¹ In the cohort of patients who present with mechanical hip symptoms, up to 76% are subsequently diagnosed with (osteo)chondral lesions of the hip joint.³²

Damage to the hip cartilage can lead to severe disabilities, onset and progression of OA, and ultimately to the need for total hip arthroplasty.³³ Given the poor regenerative properties of cartilage and the high load environment of the joint, early intervention and treatment of defects is paramount in the prevention of OA and the preservation of joint function. Due to the biomechanical relationship between a cam morphology of the femoral neck and resulting cartilage damage to the chondrolabral junction, the most common location for defects is the anterosuperior acetabulum.^{32,34} In contrast, femoral lesions are most often found centrally located in the head.³² Hip cartilage plays partially different and more extensive roles than cartilage in other joints. The concave hip articular surface provides constraint and stability, whereas the knee is aligned by ligaments and menisci, holding together joint surfaces that are otherwise not inherently constrained. The loss of joint stability and onset of cartilage degeneration in cases of acetabular fractures involving as little as 20% of the posterior wall surface, highlights the importance of hip articular surface in providing stability.³⁵⁻³⁷ Additionally, the labrum plays a key biomechanical role in providing hip stability and maintaining physiologic chondral loading. This is illustrated by the high incidence of concomitant labral pathology in the setting of chondral defects.³² Furthermore, labral tears treated with debridement instead of reconstruction, are associated with high rates of joint degeneration and the following need for arthroplasty.³⁸

<2 cm² delamination

Chondral delamination is often encountered in hip arthroscopy and commonly associated with pincer and cam-type femoroacetabular impingement (FAI).³⁹ Several techniques have been described to address and repair a chondral flap, including fibrin glue,⁴⁰ suture anchor fixation⁴¹ and scaffold implantation.⁴² Case series for each treatment option demonstrated positive clinical outcomes, while no randomized trial exists to the best of our knowledge.

Studies have reported favorable outcomes for the repair of both femoral and acetabular chondral flaps with a size of <2 cm².^{40,43} Stafford et al followed acetabular fibrin glue repairs with a second-look arthroscopy after a mean of 28 months and reported stable results.⁴⁰ Sekiya et al used a monofilament suture anchor to reattach acetabular delamination and reported good clinical outcomes.⁴¹ Notably, only 1 patient was treated and received concomitant treatment for FAI and labral tear, making the clinical results difficult to interpret. In the setting of type 2 Pipkin fractures, chondral delamination was addressed with bioabsorbable pin fixation, that was combined with rotational osteoplasty. At 4 years postoperatively, Harris Hip Score (HHS) was 99 and minimal arthritic changes were noted on radiographs.⁴⁴ Small chondral lesions have also been treated with scaffold-based repairs with resulting improved subjective patient-reported outcomes, however published results for these techniques remain limited to 2 years of follow-up.⁴⁵

While lacking a randomized in vivo trial comparing different repair techniques of chondral delamination of the hip, Cassar-Gheiti et al conducted a cadaveric biomechanical study comparing 3 fixation techniques for chondral flap injuries.⁴⁶ Cyanoacrylate repairs, fibrin glue, and suture anchor repairs were performed and underwent mechanical loading and gait cycles. Arthroscopic controls were

Table 2
Elbow.

Study	Journal	Year	Level	Enrolled participants	Lesion size (cm ²)	Age (years)	Treatment	Outcome parameter	Follow-up time	Results
Jones et al	J Pediatr Orthop	2010	IV	25	not reported	13.1	BMS	SANE, ROM	48	Significant improvement in SANE and ROM
Wulf et al	Am J Sports Med	2012	IV	10	not reported	13.9	Mfx	MEPS, ROM	42	Significant improvement in MEPS and ROM
Maruyama et al	Am J Sports Med	2014	IV	33	2.24	13.6	OATS	TaA, ROM, RTS, Rx	28.4	Significant improvement in TaA and ROM, Complete incorporation of grafts in Rx, 93.9% RTS
Lyons et al	J Shoulder Elbow Surg	2015	IV	11	>1 cm ²	14.5	OATS	DASH, ROM	22.7	Significant improvement in DASH and ROM
Uchida et al	Am J Sports Med	2015	IV	18	not reported	14.2	Fragment			
pin refixation	MEPS, ROM	39	Significant improvement in MEPS and ROM							
Mirzayan et al	J Shoulder Elbow Surg	2016	IV	9	not reported	15.3	FOCAT	MEPS, OES, DASH, VAS, ROM	48.4	Significant improvement in all scores and ROM

Abbreviations: ACI, autologous chondrocyte implantation; ADL, activities of daily living; ASES, American shoulder and elbow surgeons; BMS, Bone marrow stimulation; FOCAT, fresh osteochondral allograft transplantation; MEPS, mayo elbow performance score; Mfx, microfracture; OA, osteochondral allograft; OATS, osteochondral autograft transplantation system; OES, oxford elbow score; ROM, range of motion; RTS, return to sport; Rx, radiographs; SANE, single assessment numerical evaluation; TaS, Timmerman and Andrews score; VAS, visual analog scale.

carried out at defined cyclical intervals. Suture anchor fixation remained stable at the endpoint of 1500 gait cycles, while fibrin glue failed at an average of 27 cycles and cyanoacrylate at an average of 635 cycles.

While long-term in vivo results are lacking, it appears reasonable to repair and fix femoral and acetabular delamination $<2\text{ cm}^2$ to maintain the native chondrocytes and cartilage superstructure. The positive results of multiple refixation techniques presented above and summarized in Table 3 suggest that the repair of even a small delamination is possible and preferred over debridement.

2 to 6 cm^2 lesions

Large femoral chondral lesions without involvement of the subchondral layer can be addressed via ACI, which has shown favorable long-term results in the knee.^{47,48} However, in contrast to the knee and shoulder, the second procedure can necessitate surgical dislocation of the hip joint in order to reach and repair the cartilage defect, which can be associated with more comorbidities than an arthroscopy alone. Possible hip donor sites for use in cartilage biopsy are the non-articular femoral head-neck junction and portions of the acetabular fossa beneath the pulvinar.⁴⁹ While ACI/MACI is approved by the FDA for use in the knee, there is no current formal approval for its application in the hip. Nevertheless, initial results in the use of ACI/MACI in the hip are promising. Fontana et al compared 15 patients undergoing ACI with 15 patients treated with debridement of acetabular defects of a mean size of 2.6 cm^2 . Superior results were reported for the ACI cohort.⁵⁰ Likewise, Thier et al found significant postoperative improvements in patient reported outcomes in 29 patients undergoing MACI with a 10 month mean follow-up.⁴⁹ Krueger et al published good to excellent results for ACI in acetabular cartilage defects with an average defect size of 4.9 cm^2 in 32 patients. At a mean follow-up of 35.5 months, both mHHS (modified Harris Hip Score) and iHOT33 (international Hip Outcome Tool) were significantly improved.⁵¹ Akimau et al reported favorable outcomes after MACI-based treatment of FAI chondral defects up to 3.5 cm^2 in size at 5 years of follow-up.⁵² Despite the small number of studies available, outcomes are generally positive. The benefits of the cell-based procedures include less donor site morbidity compared to mosaicplasty and no need for allogenic tissue transplantation such as in OCA. In pathologies that involve the subchondral layer, cell-based approaches should be used with caution as they may produce inferior results as compared to structural grafts such as OATs and OCA.⁵³ In the hip, OATs donor sites with good accessibility include the ipsilateral knee or non-weight bearing areas of the femoral head. Due to OATs' ability to replace hyaline cartilage with mature structure cartilage and underlying bone rather than creating a fibrocartilage scar as with microfracture, results of OATs have been superior to microfracture in lesions sized between 2 and 6 cm^2 .⁵⁴⁻⁵⁷ Girard et al observed that full-thickness chondral defects with subchondral involvement and a mean defect size of 4.8 cm^2 demonstrated good clinical outcomes, graft integration, and a smooth chondral surface at 29 months of follow-up.⁵⁸ Similarly, Viamont-Guerra et al presented a recent series of femoral head OATs procedures with significant postoperative outcome score improvements but suggested that larger lesions ($>2\text{ cm}^2$) did not benefit as much as smaller lesions from the procedure.⁵⁹ In terms of OCA, Xin et al observed significant improvements in mHHS in 22 patients treated with OCA and low conversion rates to total hip arthroplasty despite an average lesion size of 5.43 cm^2 . Femoral cartilage lesions with a size of $>8\text{ cm}^2$ are generally considered too large for reconstruction and lead to THA in most cases (Table 2).

Table 3 summarizes studies that addressed chondral lesions of a size of 2 to 6 cm^2 . OATs and OCA are surgical options to be considered, especially in the setting of subchondral involvement and lesions $>6\text{ cm}^2$.

Knee

Patients with articular cartilage defects of the knee can experience pain and functional impairments comparable to patients with severe OA scheduled for knee arthroplasty.⁶⁰ Articular defects are identified in approximately two-thirds of all knees undergoing arthroscopy for knee pain.⁶¹⁻⁶³ Lesions with a surface area ($<2\text{ cm}^2$) are considered as small in the knee and can be silent in 1 patient but lead to symptomatic pain and accelerated joint degeneration in another.⁶¹ It remains unclear why some patients experience a significant amount of clinical symptoms, while in others, chondral injury appears silent.⁶⁴ Small defects with limited or no clinical symptoms might make larger surgeries seem excessive and unjustified; however, a wait-and-see approach, particularly as it relates to symptomatic lesions, may have negative and devastating long-term consequences. Everhart et al calculated a substantially higher risk for total knee arthroplasty in patients with full thickness cartilage defects $>2\text{ cm}^2$ compared to those with $<2\text{ cm}^2$ lesions (HR = 5.27 [95% CI = 2.70-10.3] vs HR = 2.65 [95% CI = 1.60-4.37]).⁶⁵ Regardless, thorough preoperative planning is essential when treating cartilage defects to address potential concurrent pathologies, such as tibiofemoral and patellofemoral malalignment, meniscal tears, or ligamentous instability.^{66,67} Useful diagnostic studies include dedicated knee x-rays, full-length standing hip to ankle X-rays and MRI to determine the surface and depth of the defect and possible concurrent injuries of the cruciate ligaments and menisci.⁶⁸

While the knee has the longest historic record for cartilage regeneration techniques, debridement/chondroplasty remains the most common cartilage procedure performed in the United States, estimated to comprise 66% of all cases.⁶⁹ Debridement does not aim to restore cartilage tissue but instead is palliative and aims to remove unstable flaps and create a stable articular cartilage rim surrounding any encountered defects. We believe that debridement still poses a viable, one-stage option for the treatment of small defects ($<2\text{ cm}^2$) in the presence of symptomatic mechanical blocks and resulting pain and disability. However, it is noteworthy that OATs produce favorable, long-term results in small cartilage defects, filling the lesion with viable, native hyaline cartilage.⁷⁰ OATs (and pre-drilled OCAs cores) are also logistically attractive considering that like debridement, they provide a one-stage procedure without relying on fibrocartilage scar formation. Overall, OATs/OCA is preferred over microfracture and chondroplasty in young and active patients in order to maximize long-benefits. Negative aspects of the procedure, such as high costs and donor side morbidity, still have to be taken into consideration when making a treatment decision.

Table 3
Hip.

Study	Journal	Year	Level	Enrolled participants	Mean lesion size (cm ²)	Age (years)	Treatment	Outcome parameter	Follow-up time	Results
Tahoun et al	J Arthrosc Relat Surg	2017	IV	23	3.5	40.9	Acetabular Mfx and Chitosan base scaffold repair	NAHS, iHOT33, HOS	38.5 mo	Significant improvement in all scores
Thier et al	SICOT J	2017	III	29	2.21	30.3	Acetabular MACI	iHOT33, EQ-5D, NAHS	19 mo	All scores: Significant improvement
Oladeji et al	Hip Int	2018	IV	10	3.8	24.8	Femoral head osteochondral allograft	HOOS	17.2 mo	HOOS: Significant improvement in 7/10 patients
Kilicoglu et al	Hip Int	2015	IV	1	7	27	Femoral head mosaicplasty	HHS	8 y	HHS: 55-96
Khanna et al	Bone Joint J	2014	IV	17	>3	25.9	Femoral head osteochondral allograft	HHS	41.6 mo	HHS: Significant improvement
Fontana et al	Arthrosc- J Arthrosc Relat Surg	2012	III	30	>2	40.7/42.3	Acetabular ACI vs debridement	HHS	74 mo	HHS: Significant improvement ACI group
Girard et al	Hip Int	2011	IV	10	4.8	18	Femoral head mosaicplasty	OHS HHS, Merle d'Aubigne score, UCLA score, Devane score, CT	29.2. mo	All scores improved; 6 months CT; Intact coverage
Evans et al	Clin Orthop Rel Res	2010	IV	1	5.5	32	Femoral head osteochondral allograft	HHS	12 mo	HHS: 69-94
Nousiainen et al	J Orthop Trauma	2010	V	1	>5	18	Femoral head osteochondral allograft	HHS, HOOS, MFA SF-36, VAS, MRI	46 mo	HHS: 100; HOOS: 62; MFA: 22; SF-36: 81; VAS: 0; MRI: OA changes
Maluta et al	Acta Biomed	2016	V	1	3	24	Rotational osteoplasty femoral head and bio absorbable pin fixation	MRI, HHS	4 y	HHS: 99; MRI, CT: minimal arthritic changes
Stafford et al	Hip Int	2011	IV	43	not reported	34.2	Acetabular Mfx + Fibrin glue	MHHS	28 mo	Significant improvement in MHHS
Tzaveas et al	Hip Int	2010	IV	19	not reported	36	Acetabular Mfx + Fibrin glue	MHHS	12 mo	Significant improvement in MHHS
Sekiya et al	Orthopedics	2009	V	1	not reported	17	Acetabular Mfx + Suture anchor	MHHS, HOS, CADL, HOSS	24 mo	Good results; MHHS: 96; HOSCADL: 93; HOSS: 81
Viamont-Guerra et al	Knee Surg Sports Traumatol Arthrosc	2019	IV	27	1.6 ± 0.7	28.7	Femoral head mosaicplasty	mHHS, WOMAC	12 mo	Significant improvement in mHHS and WOMAC
Zelken et al	J Orthop Trauma	2016	V	1	0.8	21	Femoral head mosaicplasty	HHS, Radiograph	8 y	HHS: 100; Radiograph: Signs of joint degeneration

Abbreviations: ACI: autologous chondrocyte implantation; CT, computerized tomography; HHS, hip harris score; HOSCADL, hip outcome score activities of daily living; iHOT33, international hip outcome tool 33; OHS, oxford hip score; Mfx, microfracture; mHHS, modified hip Harris score; MRI, magnetic resonance imaging; VAS, visual analogue scale; WOMAC, western Ontario and McMaster universities osteoarthritis Index.

Given the shortcomings of microfracture, ACI and MACI were introduced to improve the treatment of large cartilage defects ($>2 \text{ cm}^2$) of the knee.^{71,72} Consisting of 2 separate surgical procedures, harvesting chondrocytes from a non-weight-bearing surface and implantation of the cultured cartilage cells at least 3 to 5 weeks later, the procedure is associated with good outcomes that have been reported in patients at up to 2 to 9 years of follow-up.^{72,73} While second-generation ACI uses a bioabsorbable collagen membrane under which the cultured cartilage cells are injected, MACI incorporates a membrane that acts as a cell carrier to distribute the cells more evenly with a density of 500,000 to 1,000,000 cells per cm^2 .^{2,74} To date, the knee joint remains the only location where the use of ACI and MACI has been approved by both the FDA and European Medicines Agency. The relatively high costs of the treatment and its 2-stage design represent the biggest limitations to broad ACI/MACI implementation.⁷⁵

In intermediate and large lesions ($>2 \text{ cm}^2$), OATs and OCA comprise the most commonly used treatment options, at least in the US. Due to the limited availability of OCA, OATs and ACI are more commonly used in the EU. Levy et al reported a 82% survivorship after 10 years in 126 knees treated with OCA and a mean total graft surface area of 8.1 cm^2 (range, $1\text{--}27 \text{ cm}^2$).⁷⁶ Melugin et al recently described a hybrid technique involving (OATs) for the treatment of large lesion sizes with a mean of 2.8 cm^2 and reported positive outcomes at 36 months follow-up.⁷⁷

In summary, cartilage lesions of the knee (femoral condyles, trochlea, patella) typically involve a large surface area and are most commonly treated with ACI/MACI or structural grafts such as OATs and OCA. Debridement and microfracture remains in clinical use, particularly for small lesions, but evidence suggests inferior mid- and long-term results as compared to structural and biologic alternatives (Table 4).

Ankle

The ankle is a hinge joint with 3 articulating highly-congruent bones, namely the talus, tibia and fibula.⁷⁸ Mean ankle cartilage thickness ranges from 1 to 1.7 mm whereas the knee cartilage ranges from 1.5 mm to 6 mm in thickness.⁷⁹ Small deviations in anatomy predispose the ankle to osteochondral defects and arthritis. For these reasons, it is paramount to identify and appropriately treat symptomatic cartilage lesions in the ankle.

Unlike other large, weight-bearing joints, the ankle very rarely develops OA without prior, predisposing trauma.^{80,81} Once trauma occurs, ankle arthritis can become a significant source of morbidity with multiple potential treatment options.⁸² Ankle arthroplasty is a treatment option when substantial OA with multifocal chondral damage has already occurred, but the results of ankle arthroplasty are behind that seen in the knee and hip.⁸³ An alternative to arthroplasty is ankle arthrodesis, however this is associated with limited range of motion, secondary mid/hindfoot arthritis, and a relatively high risk of postoperative infection and nonunion. Cartilage repair and regeneration techniques seek to prevent arthritis in an attempt to prevent or at least substantially delay the need for arthroplasty/arthrodesis. Although multiple treatment options exist, there is limited evidence supporting 1 restorative technique over another.⁸⁴

The current consensus is that debridement or bone marrow stimulation with microfracture to produce fibrocartilage is generally employed for primary smaller defects up to 1.5 cm^2 in size.^{85–88} Several studies have investigated the treatment of talar lesions ranging from 1.0 cm^2 to 1.7 cm^2 with microfracture.^{89–93} Corr et al reported a 10-year follow-up of patients undergoing isolated arthroscopic microfracture for talar osteochondral defects, with a 93.3% survival and 85.7% return to sport rate at final follow-up. Shimozono et al suggested in a recent study that the use of an extracellular matrix cartilage allograft (EMCA) as an adjuvant to bone marrow stimulation (BMS) alone in small cartilage defects (1.5 cm^2) provides better cartilage fill than microfracture alone on MRI.⁹⁴ However, this did not translate to improved functional outcomes compared with microfracture alone at a mean follow-up time of 22 months. Choi et al investigated a possible threshold in lesion size that may exist for microfracture-based treatment. One hundred twenty ankles underwent arthroscopic microfracture for osteochondral lesion of the talus. Only 10 of 95 ankles (10.5%) with a defect area $<1.50 \text{ cm}^2$ demonstrated clinical failure.⁹⁵ In contrast patients with a defect area $\geq 1.50 \text{ cm}^2$ demonstrated a failure rate of up to 80% (20/25), highlighting the need for alternative treatment modalities for larger chondral defects.

Despite no current FDA approval, MACI is used for treatment of osteochondral lesions of the talus, particularly as it relates to larger defects. Lenz et al reported a case series of 15 patients who underwent MACI with a mean follow-up of 12.9 years. The mean size of the talar osteochondral defects was 204 mm^2 . Results were measured using the American Orthopaedic Foot & Ankle Society (AOFAS), Foot and Ankle Activity Measurement, and visual analog scale (VAS) scoring systems. A significant improvement in mean AOFAS score from 60 preoperatively to a mean of 84 at 12 years postoperatively was observed. The authors concluded that MACI is a reliable treatment method for talar osteochondral defects providing lasting pain relief and satisfying clinical results.⁹⁶ However, considering treatment costs and the need for a 2-staged procedure, the use of MACI is generally reserved for special indications in the ankle refractory to other surgical interventions.⁹⁷

Most authors consider a lesion size of 3 cm^2 as the upper limit for cartilage restoration in the ankle. DeSandis et al reported a case series of 46 patients treated for osteochondral lesions of the talus and included lesions sizes up to 5.4 cm^2 but did not report results relative to lesion size, limiting the interpretation of their results as it relates to very large ($>3 \text{ cm}^2$) lesions.⁹⁸ Table 5 summarizes the evidence currently available for the treatment of chondral defects in the ankle.

Table 6

Limitations

Apart from the knee joint, available data on treatment types depending on cartilage lesion size are limited. Prospective randomized controlled studies are not available for every joint and many available studies represent case studies with limited implications for

Table 4
Knee.

Study	Journal	Year	Level	Enrolled participants	Mean lesion size (cm ²)	Age (years)	Treatment	Outcome parameter	Follow-up time (months)	Results
Saris et al	Am J Sports Med	2009	I	118	2.4 ± 1.2 (1-5)	33.9	CCI or MF	KOOS	36	Significantly better results in CCI group, especially in patients with symptom onset <3 y
Vanlauwe et al	Am J Sports Med	2011	I	112	2.4 ± 1.2 (1-5)	33.4	CCI or MF	KOOS	76	Significantly better results in CCI group, especially in patients with symptom onset <3 y; no difference in lesion size subgroups
Saris et al	Am J Sports Med	2014	I	144	5.55	33.85	MACI or MF	KOOS	24	Cartilage defects sized ≥3 cm ² treated with MACI were statistically and clinically significantly better than MF
Knutsen et al	J Bone Joint Surg Am	2016	I	80	4.8	32.2	ACI or MF	ICRS, Lysholm, Short-Form-36, Tegner	180	Satisfactory results in 77% of patients
Volz et al	Int Orthop	2017	I	47	3.6 (2-10)	27-47	MF, AMIC glued or AMIC sutured	Mod. Cincinnati, ICRS, VAS, MRI	60	Significantly better results in both AMIC group compared to MF
Brittberg et al	Am J Sports Med	2018	I	128	5	34	MACI or MF	KOOS	60	Cartilage defects sized ≥3 cm ² treated with MACI were statistically and clinically significant better than MF

Abbreviations: ACI, autologous chondrocyte implantation; AMIC, autologous matrix induced chondrogenesis; CCI, characterized chondrocyte implantation; ICRS, international cartilage repair society scale; KOOS, knee injury and osteoarthritis score; MACI, matrix induced autologous chondrocyte implantation; MF, micro fracture; VAS, visual analog scale.

Table 5
Ankle.

Study	Journal	Year	Level	Enrolled participants	Mean lesion size (cm ²)	Age (years)	Treatment	Outcome parameter	Follow-up time (months)	Results
Gobbi et al	Arthroscopy	2006	II	21	4.4	32	Mfx, OCA, chondroplasty	AOFAS, AHS, SANE, NPI, and MRI findings	53	No significant difference in treatments, NPI was lower in Mfx and chondroplasty groups
Domayer et al	Osteoarthritis Cartilage	2012	IV	20	1.3 ± 0.4	30	Mfx, MACT	AOFAS, MRI findings, and ROI analysis	65.4	Similar results in both treatment groups
Tahta et al	J Orthop Surg	2017	IV	98	2 ± 0.3	29.3	Nfx; HACS with CBMA	AOFAS, VAS, and MOCART	41.3	Better clinical and radiological results and higher cartilage quality in HACS with CBMA technique group compared to NF
Murphy et al	Foot Ankle Surg	2019	III	101	majority of lesions < 1.5	37.1	Mfx + bone marrow aspirate concentrate + fibrin glue	VAS pain score, FAOS, and revision rate	36	Similar clinical results; Less revisions in the augmentation group
Lee et al	Am J Sports Med	2009	IV	19	2.2 ± 0.3	34.6	Mfx	AOFAS, ICRS repair grades	12	90% of ankles achieved excellent results

Abbreviations: AHS, ankle hindfoot scale; AOFAS, American orthopaedic foot and ankle society; HSS, Hannover scoring system; MOCART, magnetic resonance observation of cartilage repair tissue; MRI, magnetic resonance imaging; NPI, numeric pain intensity; RCT, randomized controlled trial; ROI, region of interest; SANE, single-assessment numeric evaluation; VAS, visual analogue scale.

Table 6
Joint overview.

Joint	Joint Load	Cartilage Thickness (mm)	Incidence of Cartilage Defects [†]	Average Lesion Size (cm ²)	Number of included Papers in this Review
Shoulder	350 N **	Glenoid: 1.5 ± 0.2; Humeral Head: 1.5 ± 0.4	5% (general population); 17% (over-head athletes)	3.2 (1.8 - 7.1)	10
Elbow	250 N*	1.63 ± 0.28	OD: 18 - 29/100.000	1.1 (0.7 - 2.2)	10
Hip	Walking: (2.8 x BW) N	Acetabular: 1.46 ± 0.17; Femoral Head: 1.78 ± 0.2	Acetabular: 14%; Femoral: 6%	3.5 (1.2 - 8.2)	19
Knee	Walking: (2.8 x BW) N	Femur: 2.34 ± 0.71; Tibia: 2.38 ± 0.9; Patella: 3.08 ± 0.94	7% under the age of 40; 9% under the age of 50	3.3 (1 - 10)	31
Ankle	Walking: (5 x BW) N	Tibia: 1.16 ± 0.14; Fibula: 0.85 ± 0.13; Talus: 2.38 ± 0.4	2 - 3%	2.3 (0.9 - 4.7)	22
Abbreviations: BW, body weight; OD, Osteochondritis dissecans; N, Newton					
*maximum activation of M. triceps					
**maximum activation of the rotator cuff					
†-data available of limited quality, values are in part calculated estimations based on incidental MRI/Arthroscopy findings					

treatment decisions. Furthermore, several studies included in this review do not differentiate between singular focal cartilage defects and defects that were simultaneously treated with concomitant injuries. Therefore, the reported results of cartilage repair might be confounded by concomitant ligament, fibrocartilage, or a boney repair.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) has been used to synthesize this study; however, reporting bias cannot be ruled out with last certainty. While all major databases have been searched, systematic reviews are still prone to evidence selection bias from potentially missed studies. This risk must be taken into consideration when translating the results from this study.

Finally, risk of bias in primary studies must be considered as in every systematic review. Each individual study included in this systematic review was assessed for key sources of bias. Selection bias, detection bias, attrition bias, and outcome reporting bias were assessed and addressed where applicable.

Conclusions

The purpose of this review was to provide guidance regarding treatment options as they relate to size and joint location of cartilage lesions. While large, symptomatic defects are often addressed with surgical intervention, relative indications are less clear in the case of small articular defects. Surgeons face a difficult decision between the possible over-treatment of small lesions with questionable clinical relevance and balancing the possible suboptimal mid- to long-term consequences of non-operative management and resulting inflammation and joint degeneration, especially in young and active patients. When conservative treatment fails to provide symptomatic relief of chondral lesions, surgical treatment and cartilage restoration is often indicated. Cartilage preservation techniques are rapidly emerging and becoming increasingly available. While the future for biologic cartilage repair and restoration is promising, to date, there is a relative paucity of studies available, especially as it relates to prospective, well-controlled, and long-term series. Despite the good to excellent results reported in numerous studies, no standardized method of lesion analysis and outcome evaluation continues to persist.

When treating joint pain associated with cartilage defects, we recommend a comprehensive and patient focused approach, using an algorithm and evidence-based support when possible. For patients without substantial improvements following comprehensive non-operative management, we recommend evaluation of cartilage lesion location and size. In general, small lesions can be treated with repair/re-fixation when possible (ie, flap repair) or debridement. In cases where repair is not possible, debridement, when combined with intraoperative lesion biopsy, can be converted to second stage ACI/MACI for symptoms refractory to debridement-based management. For larger symptomatic defects, we generally recommend consideration of ACI/MACI or structural grafts such as OATs and OCA, particularly in the setting of subchondral involvement.

In conclusion, the treatment of articular cartilage defects is highly individualized and takes into consideration lesion size, lesion depth location, and available treatment modalities. By incorporating published literature into clinical decision making and patient counselling, surgeons and patients alike can benefit from the summarized currently available data regarding the treatment of shoulder, elbow, hip, knee, and ankle chondral lesions. [Figure 2](#) provides a comprehensive summary of treatment recommendations regarding lesion sizes. We believe an awareness of emerging modalities and their currently available scientific support is imperative to the cartilage surgeon's practice, so the merit of various approaches can be evaluated and the most promising treatment option in the individual defect configuration can be found. This review assesses the currently available evidence for cartilage repair of large joints

Cartilage defects and surgical treatment

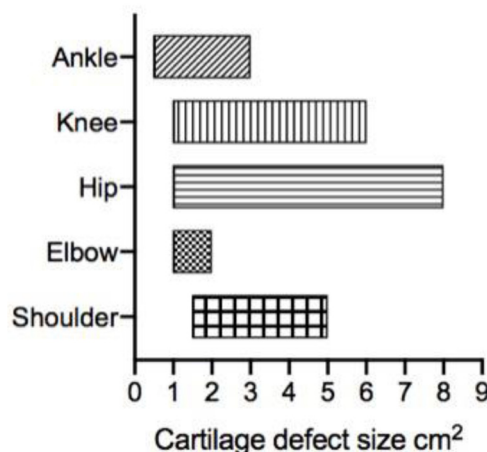


Fig. 2. Treatment recommendations per joint and lesion size.

in regard to lesion size. Further research is warranted to broaden the scientific base for clinical decisions, as high-quality evidence remains limited outside from the knee joint.

Author contributions

M.H. and D.B.F.S. designed the research. M.H. performed the literature search. M.H. wrote the manuscript in consultation with D.B.F.S., R.J.H.C., M.H., A.J.K. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

Declaration of competing interest

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

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