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Abstract

Background: Articular cartilage is a smooth, water-based cartilage that lines bone surfaces in synovial joints such as the knee and hip, providing a frictionless surface for movement and absorbing biomechanical shock. Defects of this tissue are a common cause of pain and functional impairment, yet repair of these defects remains challenging because of the poor regenerative capacity of cartilage. Hydrogel-based scaffolds are increasingly used to augment cartilage repair by supporting tissue regeneration. However, reported MRI and clinical outcomes remain heterogeneous. This systematic review and meta-analysis evaluated MRI-based and patient-reported outcomes following hydrogel-assisted cartilage repair for focal knee articular cartilage defects.

Methods: This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with the International Prospective Register of Systematic Reviews (PROSPERO). PubMed/MEDLINE, Embase, Scopus, and Cochrane CENTRAL were searched for eligible studies evaluating hydrogel-based cartilage repair in adults with focal knee cartilage defects. The primary outcome was the 12-month MOCART score. The secondary outcome was International Knee Documentation Committee (IKDC) score. Risk of bias was assessed using the Methodological Index for Non-Randomized Studies (MINORS) instrument.

Results: Seven studies, including 160 reported cartilage repair outcomes, met inclusion criteria. Pooled random-effects meta-analysis revealed a mean MOCART score of 71.2 (95% CI 66.2 - 76.2) and mean IKDC score of 70.2 (95% CI 65.5-74.9). CarGel subgroup analysis produced a pooled MOCART score of 68.9 (95% CI 65.3-72.5) and negligible heterogeneity ($I^2 = 0\%$). Leave-one-out analysis showed no substantial alteration of pooled estimates.

Conclusion: Hydrogel-based articular cartilage repair was associated with encouraging MRI based and patient-reported function, supporting the role of hydrogel scaffolds as adjuncts to marrow stimulation by helping promote reproducible early repair tissue formation. Future comparative studies should standardize imaging and clinical outcome reporting, incorporate longer term follow-up, and directly compare hydrogel biomaterial categories.

Keywords: knee; articular cartilage defect; cartilage repair; hydrogel; MOCART; magnetic resonance imaging.

Introduction

Articular cartilage defects of the knee are a common source of pain, functional limitation, and impaired activity in both active and aging populations.^[1] Since mature articular cartilage has limited vascularity and low cellularity, its capacity for spontaneous repair is poor.^[2] Untreated focal defects may therefore persist, worsen symptoms, and contribute over time to progressive joint surface degeneration and osteoarthritis.^[2,3] Despite advances in cartilage restoration, reliably regenerating durable hyaline-like cartilage that restores both structure and function remains a major clinical challenge.

These limitations have led to the development of surgical strategies designed to stimulate or support cartilage repair.^[4] For appropriately selected focal cartilage defects, microfracture is frequently used because of its technical simplicity and cost-effectiveness.^[5] However, repair tissue after microfracture is often fibrocartilaginous rather than hyaline-like, raising concerns about durability and functional recovery.^[5,6] Scaffold-assisted approaches, particularly hydrogel-based biomaterials, have therefore gained attention as adjuncts to marrow stimulation.^[7,8] By stabilizing the marrow clot and providing a matrix-like environment for early tissue formation, these scaffolds may improve the quality of cartilage repair.^[7,8] Scaffold composition may also be clinically relevant, as natural, synthetic, and hybrid biomaterials differ in their biologic and mechanical properties.^[9–13]

Although patient-reported outcomes are essential for assessing treatment success, they do not fully characterize the structural quality of repair tissue.^[14,15] MRI provides a noninvasive method for evaluating cartilage repair morphology, and the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score is widely used in cartilage restoration studies.^[16,17] Evaluation at approximately one year after surgery provides a practical early benchmark for

assessing repair tissue maturation after the initial healing period.^[18] However, published outcomes remain difficult to interpret because studies vary in scaffold composition, lesion characteristics, surgical technique, follow-up duration, and outcome reporting.^[19,20] As a result, surgeons have limited evidence to guide biomaterial selection, counsel patients regarding expected recovery, and determine whether early structural repair translates into meaningful clinical improvement. Direct comparisons between biomaterial types remain limited, and there is no clear consensus regarding the quality of cartilage repair achieved at one year after hydrogel-assisted treatment. Previous systematic reviews primarily included studies published before 2022 and focused broadly on cartilage repair techniques. Since then, several new hydrogel technologies, including UPAL and GelrinC, have emerged. Therefore, an updated synthesis of MRI-based and clinical outcomes is warranted. The purpose of this systematic review and meta-analysis was to evaluate MRI-based and patient-reported outcomes following hydrogel-based cartilage repair for focal knee articular cartilage defects, while identifying potential material-specific trends and areas requiring further investigation.

Methods

Study Design and Search Strategy

This systematic review and meta-analysis was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.^[21] The primary objective of this study was to evaluate MRI-based and patient-reported outcomes following hydrogel-assisted cartilage repair for focal chondral and osteochondral defects of the knee. Hydrogel material category was evaluated descriptively and explored when sufficient data were available. The primary outcome was the one-year MOCART score. A study protocol was developed and prospectively registered in the International Prospective Register of Systematic

Reviews (PROSPERO) under registration number CRD420261408682. The original protocol proposed comparisons among hydrogel categories, however, the available studies did not provide sufficient comparable data to support the planned group level analyses. The review scope and synthesis approach were therefore revised to reflect the available evidence.

A comprehensive literature search was performed in PubMed, Embase, Scopus, and Cochrane CENTRAL on May 30, 2026. Searches were limited to studies published from 2016-2026. The search strategy was developed using keywords related to the study objective, including terms relevant to knee anatomy, cartilage defects, hydrogel interventions, and MRI outcomes. A representative search strategy included terms such as ("knee" OR "femoral condyle") AND ("cartilage repair" OR "chondral defect") AND ("hydrogel" OR "hyaluronic acid") AND ("MRI" OR "MOCART"). This search strategy was used to capture relevant studies that addressed all aspects of the research question (Supplemental Table S1).

Eligibility Criteria

Eligible studies included adult patients with focal chondral or osteochondral defects of the knee. Studies evaluating natural or synthetic hydrogel-based therapies were eligible for inclusion. Studies were required to report MRI-based outcomes with a minimum of one year follow-up. Eligible study designs included randomized controlled trials, prospective cohort studies, retrospective cohort studies, comparative observational studies, and case series with more than one patient. Studies including pediatric populations, cadaveric specimens, animal models, or in-vitro experiments were excluded. Studies that assessed anatomical sites other than the knee or cartilage repair methods that did not incorporate a hydrogel-based intervention were excluded. Studies evaluating hydrogels seeded with growth factors, stem cells, or autologous implants were

also excluded. Additional exclusion criteria were non-English studies, reviews, protocols, editorials, abstracts, and case reports.

Study Selection

Records identified through the literature search were uploaded into Covidence, where duplicate citations were automatically identified, then manually reviewed and removed. Title and abstract screening were conducted independently (E.L. and M.S.) according to the predefined inclusion and exclusion criteria. Full-text articles were then assessed for eligibility by the same two reviewers. Discrepancies at any stage of the screening process were resolved by a third reviewer (C.S.).

Data Extraction

Three independent reviewers extracted data from the included studies using a standardized extraction template. Extracted variables included study characteristics (author, publication year, study design, and country), patient demographics (sample size, age, sex, and body mass index), lesion characteristics (location, size, and depth), intervention details (hydrogel classification, hydrogel composition, and surgical technique), and reported outcomes. Outcome measures included MOCART and IKDC scores.

Risk of Bias Assessment

Risk of bias (RoB) was assessed using the Methodological Index for Non-Randomized Studies (MINORS) instrument.^[22] Both the non-comparative and comparative versions of the MINORS tool were applied according to study design. The individual items in the MINORS instrument were scored as 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). RoB

assessment was performed independently by the second author (E.L.) and verified by the first author (C.S.).

Outcome Measures

The primary outcome was the 12-month MOCART score. When multiple MRI scoring systems were reported, only studies with sufficiently comparable numerical outcomes were included in quantitative synthesis. The secondary outcome was patient-reported IKDC scores.

Statistical Analysis

All statistical analyses were performed using R version 4.0.4 with the meta package version 8.5.0. A random-effects model was used to calculate pooled mean estimates with corresponding 95% confidence intervals (CIs). Separate meta-analyses were performed for 12-month MOCART and IKDC scores. Forest plots were generated for all quantitatively synthesized outcomes.

Statistical heterogeneity was assessed using Cochran's Q test and the I^2 statistic. I^2 values were interpreted as follows: <25% indicated low heterogeneity, 25%–50% indicated low-to-moderate heterogeneity, 50%–75% indicated moderate heterogeneity, and values exceeding 75% indicated substantial heterogeneity. Leave-one-out sensitivity analyses were performed for MOCART outcomes to evaluate the influence of individual studies on pooled estimates. Exploratory subgroup analyses were performed for studies evaluating CarGel, with the aim of assessing MRI repair outcomes within a more homogeneous biomaterial category. ^[23–25]

Results

Study Selection

The database search identified 682 articles, 96 of which were identified as duplicates and removed. The remaining 586 articles went through abstract screening according to inclusion and exclusion criteria, which resulted in 518 excluded articles, one text not retrieved due to a paywall, and 67 studies eligible for full-text screening (Figure 1). Of these, 60 studies were excluded for the following reasons: 49 studies had the wrong intervention (often including supplemental techniques such as stem cell seeding or growth factors), three had no extractable data, six had no MRI-based outcomes, one had the wrong study design, and one study predated 2016. A total of seven studies were included in the systematic review. Of these studies, five were eligible for quantitative meta-analysis of MOCART and four for IKDC outcomes.

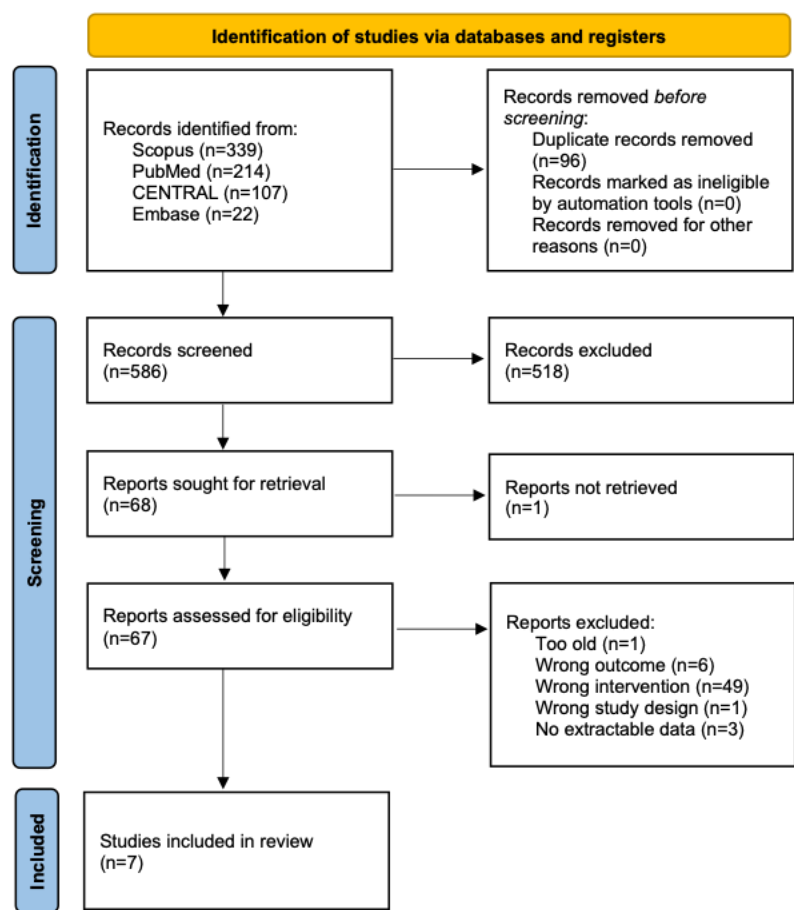


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. PRISMA flow diagram showing study identification, screening, eligibility assessment, and inclusion.

Study Characteristics

The seven eligible studies included a total of 172 patients undergoing articular cartilage repair surgery, and the final outcomes of 160 of these patients were reported (12 total patients were lost to follow-up).^[23–29] One retrospective single-arm study, one retrospective comparative study, four prospective single-arm studies, and one multicenter randomized controlled trial were identified. Two of these studies included microfracture control groups.^[23,27] Mean patient age ranged from 31-48 years old. Mean reported BMI ranged from 24.5-26.5 kg/m². Most studies included predominantly males, as well as relatively young, active adults with symptomatic focal cartilage defects. Study characteristics are described in Table 1.

Table 1. Characteristics of Included Studies, Patient Cohorts, and Cartilage Lesions.

Study	Group	N	Mean Age	Female, n/N (%)	Mean lesion size and location	Hydrogel composition	Natural vs synthetic classification	Surgical technique
Calvo et al., 2021	CarGel + MF	15	33.8 ± 9.9	2/15 (13.3)	1.99 cm ² [1.1–3.8]. Trochlea and patella	Chitosan scaffold mixed with autologous whole blood	Natural	Arthroscopic
Glasbrenner et al., 2020	Chondrotissue + MF	12	47.9 [35–68]	6/12 (50.0)	1.7 cm ² , [0.5–3.0 cm ²]. Femoral condyle	Polyglycolic acid scaffold with sodium hyaluronate, fixed with polylactic acid pins	Hybrid	Arthroscopic
Glasbrenner et al., 2020	MF alone	12	36.7 [22–66]	3/12 (25.0)	1.7 cm ² , [0.5–3.0 cm ²]. Femoral condyle	No hydrogel or scaffold comparator	Control, no hydrogel	Arthroscopic
De Marziani et al., 2024	CarGel + MF	13	31.3 ± 12.7	4/13 (30.8)	3.0 ± 0.8 cm ² . Patella	Chitosan-based scaffold	Natural	Arthrotomy
Ozturk et al., 2023	CarGel + MF	21	32.5 overall [19–44]; group-specific NR	13/38 overall (34.2); group-specific NR	2.9 ± 0.4 cm ² . Femoral condyle	Chitosan-based liquid bioscaffold	Natural	Arthroscopic
Ozturk et al., 2023	MF alone	17	32.5 overall [19–44]; group-specific NR	13/38 overall (34.2); group-specific NR	3.0 ± 0.4 cm ² . Femoral condyle	No hydrogel or scaffold comparator	Control, no hydrogel	Arthroscopic
Poggi et al., 2023	CARGEL + MF	14	31.8 ± 11.9	5/14 (35.7)	2.9 ± 1.0 cm ² . Patella	Chitosan solution, buffer, and autologous whole blood	Natural	Arthrotomy
Schreiner et al., 2020	GelrinC + MF	56 enrolled; 44 with 12-	38 ± 10	20/56 (35.7)	2.42 ± 1.08 cm ² . Femoral condyle	Polyethylene glycol diacrylate plus	Hybrid	Arthroscopic and mini-arthrotomy

		mo				denatured human fibrinogen		
		MOCART						
Onodera et al., 2023	UPAL gel + MF	12	33.1 [16–48]	4/12 (33.3)	1.81 ± 0.70 cm ² . Medial or lateral femoral condyle, trochlea, and patella	2% sodium alginate solution derived from ultra-purified alginate	Natural	Arthroscopic

Abbreviations: MF, microfracture; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue; MRI, magnetic resonance imaging; NR, not reported; UPAL, ultra-purified alginate.

[] Denotes range; +/- denotes standard deviation.

For comparative studies, intervention and control cohorts are listed in separate rows beneath the same study.

Ozturk et al. did not have group-specific age and sex extracted, so overall age and sex are shown for both groups.

Lesion Characteristics

Lesion locations included lateral and medial femoral condyles, patella, and trochlea. Three studies solely included femoral condyle lesions, two studies included solely patellar chondral lesions, one study included patellar and trochlear chondral lesions, and one study included all of the above lesion locations. Mean lesion size range was (1.7-3.0 cm²) across studies. Reported chondral defect etiologies included traumatic lesions, osteochondritis dissecans, and focal degeneration.

Hydrogel Interventions and Surgical Techniques

Five studies included natural hydrogels. Four of these used CarGel, a chitosan-based scaffold.^[23–26] The remaining study used Ultra-Purified Alginate Gel, or UPAL.^[28] Two studies included semi-synthetic/hybrid scaffolds. Glasbrenner et al. included surgeries with Chondrotissue, a hybrid hydrogel made from polyglycolic acid and sodium hyaluronate fixed with polylactic acid pins.^[27] Schreiner et al. included the hybrid hydrogel GelrinC, made from polyethylene glycol diacrylate (PEG-DA) and denatured human fibrinogen.^[29] Microfracture was performed concomitantly in all studies to stimulate the bone marrow. Most procedures were arthroscopic in nature, although several studies reported open arthrotomy. Follow-up durations ranged from approximately 3-80 months, with all studies reporting outcomes at 12 months.

Risk of Bias Assessment

Overall, the included studies demonstrated predominantly moderate RoB with MINORS scores generally ranging from 8-13/16 (using the scale for noncomparative studies) and 15-20/24 (using the scale for comparative studies). Common methodological limitations included small sample sizes, lack of a priori sample size calculation, absence of control groups in case series, retrospective study design, and incomplete reporting of patient enrollment or attrition. However, many studies incorporated validated clinical outcome measures, MRI-based assessments, and appropriate follow-up periods, with one comparative study further strengthened by blinded imaging evaluation. Supplemental Table S2 includes individual study RoB scores.

MOCART Outcomes

Five studies including 106 total patients reported 12-month MOCART scores.^[23–25,28,29] The four non-comparative studies had a mean RoB score of 11/16 and the one comparative study had a RoB of 15/24. Pooled random-effects meta-analysis revealed a mean MOCART score of 71.2 (95% CI 66.2 - 76.2) (Figure 2). Moderate heterogeneity was observed ($I^2 = 66.8\%$). Leave-one-out sensitivity analysis showed that exclusion of individual studies did not substantially alter the pooled estimates (Supplemental Figure S1). Exclusion of Schreiner et al. article produced the greatest change in mean MOCART score pooled estimates (71.2 to 68.7) and eliminated all heterogeneity ($I^2 = 0\%$). Exploratory analysis of CarGel hydrogel subtypes was performed, resulting in a pooled MOCART score of 68.9 (95% CI 65.3-72.5) and negligible heterogeneity ($I^2 = 0\%$) (Supplemental Figure S2).

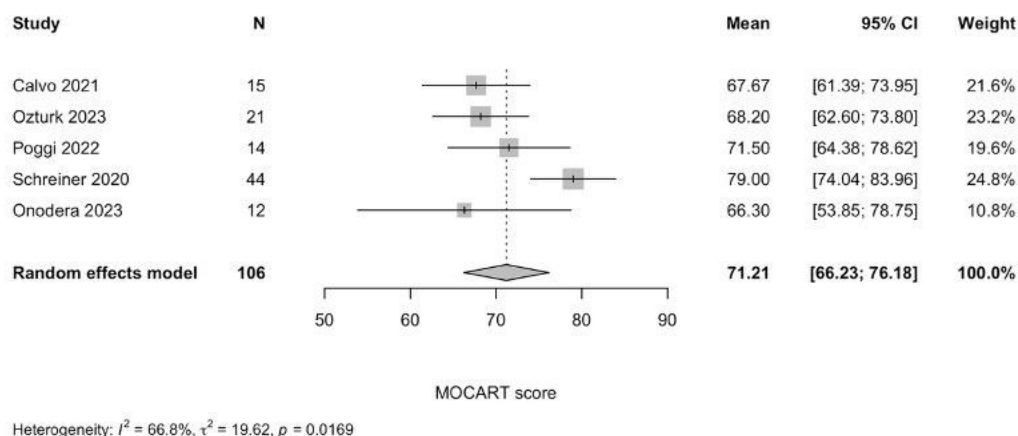


Figure 2. Forest plot of 12-month MOCART score.

IKDC Outcomes

Four studies including 51 total patients had extractable 12-month IKDC score data.^[25–28] The three noncomparative studies had a mean RoB score of 11.7/16 and the one comparative study had a mean RoB score of 20/24. Meta-analysis resulted in a pooled IKDC score of 70.2 (95% CI 65.5–74.9) (Figure 3). Negligible between-study heterogeneity was observed ($I^2 = 0\%$).

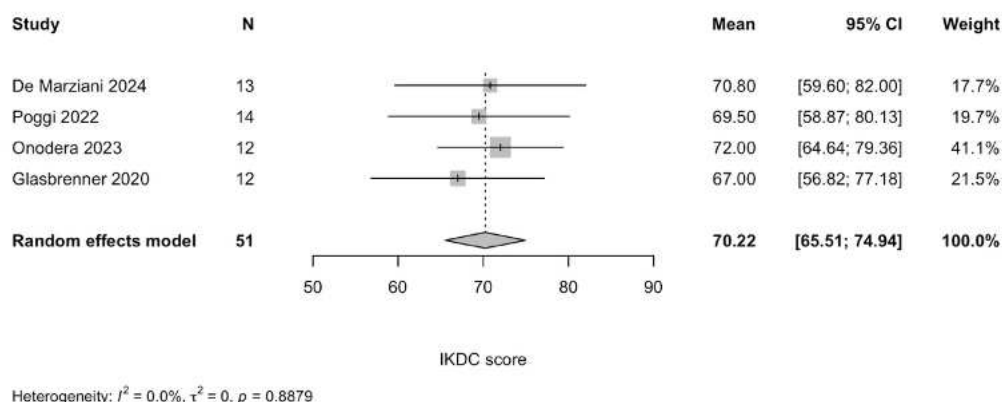


Figure 3. Forest plot of 12-month IKDC score.

Discussion

Principal Findings

The main finding of this paper was the association of hydrogel-based articular cartilage repair with moderate to favorable MRI repair tissue quality. This is reflected by a pooled mean 12-month MOCART score of 71.2. The secondary outcome investigated in this study was also generally favorable, evidenced by a pooled mean IKDC score of 70.2. Heterogeneity of results differed by outcome. MOCART score showed moderate heterogeneity, while IKDC showed negligible heterogeneity.

MOCART Outcomes

The pooled MOCART score was 71.2, suggesting favorable structural and morphological repair after hydrogel-assisted cartilage repair, but not complete restoration of native cartilage architecture. Leave-one-out analysis showed that the pooled estimate remained relatively stable after removal of most individual studies, with pooled means ranging from 72.2 to 73.4. Schreiner et al. was the exception. Removing this study decreased the pooled mean to 68.7 and eliminated heterogeneity, suggesting that it was a major contributor to both the higher pooled MOCART estimate and the observed between-study variability. This finding is notable because Schreiner et al. evaluated GelrinC, a hybrid hydrogel composed of polyethylene glycol diacrylate and fibrinogen.^[29] This hybrid design may differ from other scaffold materials by pairing the structural properties of a synthetic hydrogel with a biologic component intended to support cellular attachment and tissue integration. The influence of this study suggests that scaffold composition may be an important factor in MRI-based repair quality. Clinically, this is relevant because successful cartilage repair depends not only on defect filling, but also on forming repair tissue that can integrate with surrounding cartilage and tolerate mechanical loading over time. To contextualize the clinical relevance of the pooled MOCART score, a prior study of 111 patients undergoing non-hydrogel cartilage repair techniques,

including minced cartilage implantation, autologous cartilage implantation, minced cartilage with platelet-rich plasma, and microfracture, reported a mean MOCART score of 58 and MOCART 2.0 score of 66 at a mean follow-up of 15.3 ± 14.0 months.^[30] In comparison, the pooled 12-month MOCART score in the present review was 71.2, suggesting that hydrogel-assisted repair may be associated with favorable MRI-based repair tissue quality. In practice, this may support the role of hydrogel scaffolds as adjuncts for improving early structural repair after cartilage surgery. However, this comparison is indirect and should not be interpreted as evidence of superiority because of differences in patient populations, lesion characteristics, surgical techniques, and follow-up duration.

CarGel Exploratory Subgroup Analysis

Exploratory analysis of CarGel studies produced a pooled mean MOCART score of 68.9 with negligible heterogeneity ($I^2 = 0\%$). Clinically, this suggests that when CarGel is used as an adjunct to marrow stimulation, MRI-based repair morphology is relatively consistent and indicative of integration and tissue regeneration.

For surgeons, this finding may be useful when counseling patients that CarGel-assisted microfracture is associated with reproducible short-term structural repair findings, while recognizing the small sample size of this study does not allow for a high degree of certainty.

Relationship Between Structural Outcomes and Clinical Outcomes

The pooled mean IKDC score of 70.2 demonstrates moderately favorable patient-reported function after hydrogel-assisted cartilage repair. Additionally, negligible heterogeneity indicates IKDC scores were consistent across the included studies. However, this pooled postoperative score should be interpreted as a measure of functional status rather than direct evidence of the magnitude of clinical improvement. For context, Oetli et al. reported a mean pooled IKDC score

of 48 ± 14 across 111 knee articular cartilage repairs using Minced Cartilage Implantation, Autologous Cartilage Implantation, Minced Cartilage with Platelet-Rich Plasma, or microfracture.^[30] Although this comparison is indirect and limited by differences in patient populations, procedures, lesion characteristics, and follow-up duration, it places the present pooled IKDC score within an encouraging clinical range.

Clinically, these findings suggest that hydrogel-assisted cartilage repair may be associated with encouraging short-term patient-reported function. However, current evidence does not establish whether hydrogel-based approaches are superior to alternative cartilage repair strategies or identify which patients are most likely to benefit.

Hydrogel Type and Material-Specific Interpretation

The available comparative literature does not support a single hydrogel material for all patients with focal knee articular cartilage lesions.^[31] Until this evidence becomes available, hydrogel composition should be considered one component of treatment selection, alongside lesion location, defect size, patient activity level, surgical approach, and the need for concomitant procedures. When selecting a hydrogel, factors to consider include biomechanics, biocompatibility, degradation rates, and tissue integration. Synthetic hydrogels offer favorable biomechanics, particularly strength, while natural hydrogels boast higher rates of integration and biocompatibility. Hydrogel composites may be the superior choice for cartilage repair, because they combine synthetic and natural materials to obtain superior mechanical and biological properties. For example, Bai et al. demonstrated that dual-network hydrogel systems can enhance tissue regeneration in a preclinical biomaterial model, supporting the broader rationale for composite scaffold development.^[32] Taken together with the findings of this paper, hybrid hydrogels are a promising area of future investigation for optimal articular cartilage repair.

Limitations and Future Directions

Evidence supporting hydrogel augmentation for articular cartilage repair remains limited. Most available data are derived from small observational studies, with few comparative investigations. Interpretation of these studies' findings is further complicated by substantial heterogeneity in lesion characteristics, surgical techniques, hydrogel composition, concomitant procedures, and outcome assessment methods, including the use of different MOCART scoring systems. Additionally, all included studies evaluated hydrogels in conjunctions with microfracture, making it difficult to isolate the independent effects of hydrogel augmentation. Variable reporting of secondary outcomes also limited quantitative synthesis and reduced the strength and generalizability of pooled conclusions. Because fewer than ten studies were included, formal assessment of publication bias (e.g., funnel plots or Egger's regression) was not performed, consistent with current methodological recommendations. Although current evidence suggest that hydrogel augmentation may improve structural and clinical outcomes following cartilage repair, future studies should focus on defining which hydrogel formulations and patient populations derive the greatest clinical benefit rather than solely accumulating observational data. Prospective multicenter comparative studies with longer follow-up should employ standardized imaging and clinical outcome measures. Future studies should also directly compare hydrogel biomaterial categories, particularly synthetic hydrogels, to better establish their role in articular cartilage repair.

Conclusion

This systematic review and meta-analysis demonstrates that hydrogel-assisted cartilage repair is associated with favorable short-term structural and clinical outcomes for focal knee articular cartilage lesions. Across included studies, hydrogel-based repair produced a pooled 12-month

MOCART score of 71.2 and pooled IKDC score of 70.2, indicating generally favorable tissue morphology and patient-reported function. These findings support the potential role of hydrogel scaffolds as clinically useful adjuncts to marrow stimulation by helping promote reproducible early repair tissue formation. CarGel studies demonstrated consistent encouraging MOCART outcomes with negligible heterogeneity, while the highest individual 12-month MOCART score was reported in the hybrid hydrogel GelrinC study. However, the current evidence base remains insufficient to establish superiority of one hydrogel class over another. Therefore, hydrogel selection should remain patient-specific, considering lesion characteristics, surgical approach, patient activity demands, and material properties.

List of Abbreviations

Magnetic Resonance Imaging (MRI), Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), International Prospective Register of Systematic Reviews (PROSPERO), International Knee Documentation Committee (IKDC), Risk of bias (RoB), Methodological Index for Non-Randomized Studies (MINORS), Body Mass Index (BMI), Ultra-Purified Alginate Gel (UPAL), polyethylene glycol diacrylate (PEG-DA)

Declarations

Ethics approval and consent to participate

Not applicable. This systematic review and meta-analysis used data from previously published studies and did not involve new human participants, human tissue, or individual patient-level data.

Consent for publication

Not applicable. This manuscript does not contain identifiable individual person's data.

Availability of data and materials

No new patient-level datasets were generated. All extracted study-level data used for analysis were derived from previously published studies cited within the manuscript.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization, M.L., J.W., I.M.; Methodology, C.S., E.L., M.S., J.G., A.S.; Software, C.S.; Validation, C.S.; Formal analysis, C.S.; Investigation, C.S., E.L., M.S.; Data curation, C.S., J.G., A.S., J.T.W.; Writing—original draft, C.S., E.L., M.S., A.S., J.G., J.T.W.; Writing—review and editing, all authors; Visualization, C.S., J.W., I.M.; Supervision, M.L., F.V., J.W., I.M.; Project administration, M.L., F.V. All authors reviewed and approved the final manuscript.

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486 **Figure Legends**

487 Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow
488 diagram. PRISMA flow diagram showing study identification, screening, eligibility assessment, and
489 inclusion. Figure 2. Forest plot of 12-month MOCART score.

490 Figure 3. Forest plot of 12-month IKDC score.

491 Figure S1. Forest plot of Leave-One-Out Sensitivity Analysis for 12-Month MOCART Score

492 Figure S2. Forest plot of CarGel-Only Exploratory Analysis for 12-Month MOCART Score

493

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