SYSTEMATIC REVIEW

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Short- to Midterm Clinical Outcomes After Autologous Minced Cartilage Implantation for Focal Chondral Defects of the Knee Are Comparable to Microfracture and Autologous Chondrocyte Implantation: A Systematic Review

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Purpose: To evaluate the safety and efficacy of autologous minced cartilage implantation (AMCI) compared with microfracture (MFX) and autologous chondrocyte implantation (ACI)/matrix-assisted ACI (MACI).
Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, PubMed, Embase, and Cochrane databases were queried in May 2025. Inclusion criteria were Level I to IV human studies published between 2015 and 2025 with ≥12-month follow-up and reporting ≥2 validated clinical outcomes. Analysis of patient cohorts was performed using forest plots to make qualitative assessments, whereas descriptive statistics and ranges were used to report quantitative data to avoid heterogeneous pooling.
Results: A total of 41 studies (2116 patients) were included. Of these, 1590 underwent ACI/MACI, 302 MFX, and 224 AMCI. The mean patient age was 34.4 years for ACI/MACI, 45.0 years for MFX, and 32.7 years for AMCI. The mean follow-up was 61.1 months for ACI/MACI, 58.6 months for MFX, and 29.3 months for AMCI. Overall, there were no significant differences between International Knee Documentation Committee, Knee Injury and Osteoarthritis Outcome Score subscores, Lysholm, Tegner, and Visual Analog Scale pain at postoperative follow-up after ACI, MACI, MFX, and AMCI. Most relevantly, there was no significant difference between International Knee Documentation Committee for ACI (50.91-92.70), MACI (34.18-89.57), MFX (37.63-79.53), and AMCI (56.97-87.29). Qualitative analysis suggests that failure was lowest in AMCI (0%) compared with MFX (1.32%) and ACI/MACI (3.21%), and reoperation rates were variably reported but tended to be lower in AMCI and MFX (n = 10 and n = 14, respectively) compared with ACI/MACI (n = 155).
Conclusions: AMCI shows clinical outcomes that are at least comparable to ACI, MACI, and MFX and may be an appropriate alternative treatment for focal chondral defects of the knee. However, available studies are heterogeneous, and long-term data for AMCI remain limited.
Level of Evidence: Level IV, systematic review of Level I to IV studies.

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Because articular cartilage defects of the knee are a frequently recognized cause of knee pain that can lead to functional deficits and the development of early osteoarthritis and disability, a shift toward developing effective surgical strategies has become an important focus. The spectrum of surgical treatments ranges from

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reparative to reconstructive approaches, with microfracture (MFX) representing 1 of the first developed and initially the most used techniques. However, the repair tissue formed after MFX is predominantly fibrocartilage, which is biomechanically inferior to native hyaline cartilage, and outcomes have been reported to decline over time.[1] Therefore, contemporary approaches to cartilage treatment have investigated cell-based cartilage repair techniques, including autologous chondrocyte implantation (ACI), matrix-assisted ACI (MACI), and more recently autologous minced cartilage implantation (AMCI), which aim to restore more anatomic, hyaline-like cartilage.

Indeed, numerous studies have shown that ACI, and more recently MACI, can achieve sustained improvements in pain, function, and quality of life, particularly at longer-term follow-up, with lower rates of deterioration compared with MFX.[2] Nonetheless, these approaches have significant limitations. For example, they both require 2 procedures, are associated with increased morbidity and rehabilitation burden, and are costly because of the cell culture process and specialized facilities required.[2] Therefore, alternative solutions to cartilage treatment that can overcome these limitations remain an area of interest with important clinical and financial implications.

AMCI has emerged as an innovative single-stage option for the treatment of focal chondral defects. This technique involves harvesting small amounts of healthy cartilage from nonweight-bearing areas, mechanically mincing it into small fragments, and reimplanting the fragments directly into the chondral defect and securing it with fibrin glue. The minced fragments contain viable chondrocytes capable of migrating and producing new extracellular matrix, with the goal of forming hyaline-like repair tissue in situ.[3-5] AMCI seeks to combine the advantages of a single-stage and minimally invasive approach that can be done arthroscopically or through smaller incisions with the biological promise of cell-based therapy while avoiding the cost and complexity of laboratory expansion.[6] It should be noted that the recovery of AMCI is similar to that of ACI/MACI.[3] Early clinical series and short-term follow-up studies have reported encouraging improvements in patient-reported outcomes, return to sport, and magnetic resonance imaging evidence of defect filling.[7-9] However, data remain limited and durability has not yet been established.

Direct comparative evidence involving AMCI with established cartilage treatments is scarce, with only limited case series and early outcomes reported to date. Surgeons treating symptomatic cartilage defects must choose between treatment modalities that vary widely in invasiveness, cost, and biological rationale, often without strong comparative evidence to guide decision-making.[10,11] Patients may be appropriate candidates for multiple techniques, yet optimal selection is hindered by limited data on how newer single-stage procedures perform relative to long-standing standards.[12] Consequently, the role of AMCI relative to established treatments remains uncertain.[7,8] Dasari et al. showed promising outcomes of AMCI compared with other single-stage techniques; however, this study failed to provide a broader comparison to commonly used 2-stage approaches; additionally, further AMCI studies have been published in recent years.[13] As such, there is a need for a synthesis of contemporary evidence comparing AMCI to established treatments to help define the relative efficacy of the procedure and to determine if it has a role in the contemporary cartilage treatment algorithm. The purpose of the current study was to evaluate the safety and efficacy of AMCI compared with MFX and ACI/MACI. The authors hypothesized that AMCI would confer comparable clinical outcome improvement at short- to midterm follow-up.

METHODS

Search Strategy and Data Extraction

The literature search was conducted according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and was registered with PROSPERO (CRD420251145815). On May 19, 2025, a comprehensive literature search of PubMed, EMBASE, and Cochrane library was conducted for studies reporting clinical outcomes related to the following treatment groups: AMCI, MFX, ACI, and MACI. The search criteria for all treatment groups included the following keywords combined with Boolean operators: “knee,” “chondral,” “osteochondral,” “articular cartilage,” “cartilage defect,” and “focal cartilage”. The following respective treatment-specific keywords were included: “autologous minced cartilage,” “minced cartilage,” “autocart,” “Microfracture,” “marrow stimulation,” “subchondral drilling,” “Abrasion Arthroplasty,” “autologous chondrocyte implantation,” “matrix-associated chondrocyte implantation,” “matrix associated chondrocyte implantation,” “ACI,” and “MACI.”

Inclusion criteria were Level I to IV papers published in English and involving human subjects. Studies published between 2015 and 2025 were included if they reported a minimum 12-month follow-up and at least 2 of the following patient-reported outcome measures (PROMs) related to knee pain or function: Knee

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Injury and Osteoarthritis Outcome Score (KOOS) subscores, International Knee Documentation Committee (IKDC), Lysholm, Tegner, and Visual Analog Scale (VAS). Exclusion criteria included nonhuman studies, interventions including juvenile or cartilage autograft implantation system or osteochondral grafting, revision cartilage surgery, and studies reporting less than 2 of the aforementioned PROMs. Biomechanical studies, in vitro/cadaveric studies, radiologic-only studies, letters to editors, nonfull-text articles, case reports, meta-analyses, review articles, and studies with follow-up periods less than 12 months were also excluded. Osteochondral autograft transfer was excluded because it involves transplantation of intact osteochondral tissue rather than cell-mediated in situ cartilage repair, representing a fundamentally different biological mechanism from the cell-based techniques (ACI, MACI, and AMCI) and marrow stimulation (MFX) evaluated herein. Similarly, the cartilage autograft implantation system was excluded as its proprietary scaffold composition differs sufficiently from standard AMCI to warrant separate evaluation.

Of the 1171 unique studies identified through the initial database search, 106 studies were screened for full-text review, yielding 41 studies (Figure 1). For studies reporting more than 1 treatment arm meeting inclusion and

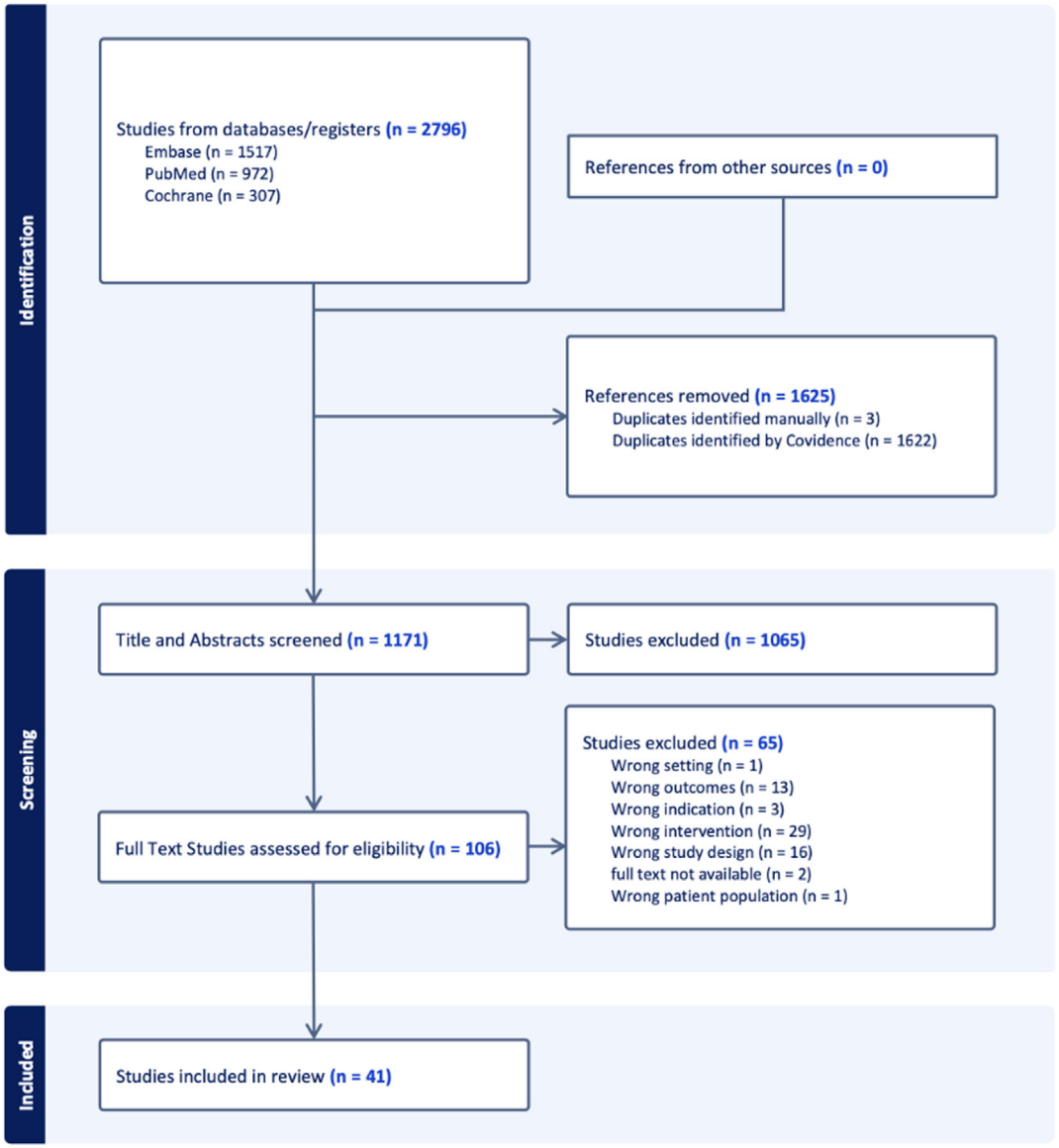

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. A total of 1171 records were identified through database searches of PubMed, EMBASE, and Cochrane. After screening, 41 studies (2116 patients) met inclusion criteria and were included in the final qualitative synthesis.

exclusion criteria, each arm was extracted and analyzed as an independent study group. Data were extracted from each study's methods and results and manually entered into a Microsoft Excel workbook (Version 2505, Microsoft, Redmond, WA). Two authors (B.E.C., K.S.S.) reviewed abstracts and full-text articles independently, and a third author (J.E.J.) resolved any discrepancies.

Data Extraction and Outcomes of Interest

Variables of interest included lead author's name, publication year, level of evidence (LOE), patient demographics, mean follow-up time, treatment group, failure and complication rate, all available PROMs data at the final follow-up, and study limitations. Adverse events including complications, reoperations, and failure were recorded if reported. Given the heterogeneity of failure definitions, failure was recorded if stated and qualitatively analyzed; no additional failure definition was analyzed because of the heterogeneity in data reporting among studies.

Risk of Bias

Two authors (B.E.C., K.S.S.) independently assessed the risk of bias using the Methodological Index for Non-Randomized Studies criteria and Cochrane Risk of Bias 2.0 (Tables 1 and 2). Any discrepancies were resolved by a third investigator (J.E.J.). The Methodological Index for Non-Randomized Studies criteria use a numerical scale with 8 items for noncomparative, nonrandomized studies and 12 items for comparative, nonrandomized studies.[14] Each item is scored as follows: 0 if not reported, 1 if reported but inadequate, and 2 if reported adequately. The maximum possible score is 16 points for noncomparative studies and 24 points for comparative studies, with a score $\geq$9 deemed an acceptably low risk of bias for noncomparative studies and $\geq$13 for comparative studies. For randomized controlled trials (RCTs), risk of bias was assessed using the Risk of Bias 2.0 tool across its 5 domains (randomization, deviations from interventions, missing outcome data, outcome measurement, and selection of reported results), with judgments classified as low risk, moderate risk, or high risk of bias based on established criteria.

To mitigate bias in data analysis, all treatment cohorts were treated as independent treatment outcomes. As such, data like PROMs were organized by treatment arms, and any treatment cohorts that did not act independently of others (e.g., crossover arms and 2 modality arms) were excluded from data extraction. Assessing risk of bias along with other metrics of study quality (e.g., LOE and statistical power) is important to contextualize results when interpreting studies as individual results and when combining them to generate insights from systematic review.[53]

Data Analysis

Forest plots of PROMs were used for qualitative analysis when both mean and standard deviation were reported. Otherwise, failure, reoperation, and adverse events were analyzed. For each PROM of interest, heterogeneity among treatment cohorts was assessed using the I^2 statistic. A high risk of bias was expected given the differences in surgical techniques, patient populations, surgeon experience, follow-up, and reported outcome measures. Thus, heterogeneity of *treatment arms* for each PROM was intentionally reported for transparency. Because of the nonrandomized nature of most included studies and potential for heterogeneity and methodological bias, pooled data analysis was not performed to avoid misleading conclusions. Likewise, pooled weighted means were intentionally removed from forest plots to avoid misleading summary estimates; given that the included studies varied substantially in design (66% noncomparative), sample size, follow-up duration, and surgical technique, a single pooled estimate would imply a level of precision not supported by the underlying data and could obscure clinically meaningful variation between individual studies, consistent with Cochrane Handbook guidance for reviews with substantial clinical and methodological heterogeneity.[54] Instead, ranges for each outcome were reported, and a qualitative assessment was conducted by examining the confidence intervals of individual studies to interpret the differences between MFX, ACI, MACI, and AMCI. Forest plots were generated using RStudio (Boston, MA).

RESULTS

A total of 41 studies, comprising 51 unique treatment arms and 2116 patients, were included in the final analysis. Among these patients, 1590 were in the ACI/MACI group, 302 in the MFX group, and 224 in the AMCI group. The mean patient age was 34.4 years (range, 12-74) for ACI/MACI, 45.0 years (range, 18-66) for MFX, and 32.7 years (range, 14-61) for AMCI. All groups met the inclusion criterion of a minimum 12-month follow-up. Across included studies, mean follow-up durations ranged from 12 to 217 months for ACI/MACI, 14 to 66 months for AMCI, and 24 to 132 months for MFX, with corresponding mean durations of 61.1, 29.3, and 58.6 months, respectively.

TABLE 1 MINORS Criteria Scores for all Included Studies

Author and Year	1. A Clearly Stated Aim	2. Inclusion of Consecutive Patients	3. Prospective Collection of Data	4. Endpoints Appropriate to the Aim of the Study	5. Unbiased Assessment of the Study Endpoint	6. Follow-Up Period Appropriate to the Aim of the Study	7. Loss to Follow-Up Less Than 5%	8. Prospective Calculation of the Study Size	Items 9-12 for Comparative Studies Only	9. An Adequate Control Group	10. Contemporary Groups	11. Baseline Equivalence of Groups	12. Adequate Statistical Analyses	Total Score	Maximum Score Possible
Akgun et al. 2015[15]	2	0	2	2	2	2	0	2						12	16
Andriolo et al. 2019[16]	2	2	1	2	1	2	1	0						11	16
Barbaret et al. 2025[17]	2	2	1	2	1	2	1	0						11	16
Behrendt et al. 2024[18]	2	0	0	2	1	2	0	2						9	16
Berruto et al. 2017[19]	2	1	2	2	1	2	1	0						11	16
Binder et al. 2021[20]	2	1	0	2	1	2	1	0						9	16
Bumberger et al. 2024[21]	2	2	0	2	1	2	1	2		2	2	2	2	20	24
Carey et al. 2020[22]	2	2	0	2	1	2	0	0						9	16
Cvetanovich et al. 2017[23]	2	2	1	2	1	2	0	1						11	16
Dai et al. 2021[24]	2	2	2	2	1	2	2	0						13	16
Ebert et al. 2017[25]	2	2	2	2	1	2	0	2						13	16
Ebert et al. 2015[26]	2	2	2	2	1	2	1	2						14	16
Gobbi et al. 2015[27]	2	2	2	2	1	2	2	0						13	16
Heinz et al. 2023[28]	2	2	0	2	1	2	0	2						11	16
Kreuz et al. 2019[29]	2	2	0	2	1	2	0	0						9	16
Matsushita et al. 2022[30]	2	1	2	2	1	2	0	0						10	16
Mayr et al. 2025[31]	2	1	0	2	1	2	0	1		2	2	2	2	17	24
Niemeyer et al. 2023[32]	2	2	1	2	1	2	0	0		2	2	2	2	18	24
Niethammer et al. 2022[33]	2	2	2	2	1	2	0	1		2	2	2	2	20	24
Pellegrino et al. 2016[34]	2	1	0	2	1	2	1	0						9	16
Retzky et al. 2024[35]	2	2	0	2	1	2	0	0						9	16
Rosa et al. 2016[36]	2	1	0	2	1	2	1	0						9	16
Runer et al. 2023[8]	2	2	1	2	1	2	1	2						13	16
Schneider et al. 2024[7]	2	0	2	2	1	2	0	0						9	16
Schneider et al. 2025[37]	2	1	2	2	1	2	0	2		2	2	2	2	20	24
Siebold et al. 2018[38]	2	2	1	2	1	2	0	0						10	16
Silva et al. 2020[39]	2	2	1	2	1	2	0	0						10	16

TABLE 1 (Continued)

Author and Year	1. A Clearly Stated Aim	2. Inclusion of Consecutive Patients	3. Prospective Collection of Data	4. Endpoints Appropriate to the Aim of the Study	5. Unbiased Assessment of the Study Endpoint	6. Follow-Up Period Appropriate to the Aim of the Study	7. Loss to Follow-Up Less Than 5%	8. Prospective Calculation of the Study Size	Items 9-12 for Comparative Studies Only	9. An Adequate Control Group	10. Contemporary Groups	11. Baseline Equivalence of Groups	12. Adequate Statistical Analyses	Total Score	Maximum Score Possible
Uchio et al. 2024[40]	2	1	0	2	1	2	0	1						9	16
van Duijvenbode et al. 2016[41]	2	2	0	2	1	2	0	0						9	16
Weishorn et al. 2024[42]	2	2	2	2	1	2	1	1						13	16
Wodzig et al. 2022[9]	2	2	1	2	1	2	0	0						10	16
Yoon et al. 2019[43]	2	1	0	2	1	2	0	1						9	16

Note: Each Domain Represents a Specific Methodological Criterion, With Color Coding Indicating the Overall Judgment of Risk (2 = Low Risk, 1 = Some Risk, 0 = High Risk).
MINORS, Methodological Index for Non-Randomized Studies.

A total of 41 studies were included in the final analysis, 10 of which contained 2 distinct treatment arms that independently met the inclusion criteria. Therefore, each arm was analyzed as a separate cohort, resulting in 51 total cohorts: 35 within the ACI/MACI group (17 ACI and 18 MACI), 9 within the MFX group, and 7 within the AMCI group.[7-9,15-52]

Patients who underwent ACI were treated with a wide range of first-, second-, and third-generation ACI techniques, including periosteum-, collagen-, spheroid-, hydrogel-, and scaffold-based variations. Patients who underwent MACI received matrix-associated ACI with various scaffolds and membranes, most commonly collagen-based, spheroid, hydrogel, or periosteum-covered implants. Although MACI is considered a third-generation ACI technique, for the purposes of this review, studies were classified according to the terminology used by the original authors. The AMCI group underwent 1-stage minced cartilage repair using fibrin glue, platelet-rich plasma, or a combination of both, with 138 patients specifically treated using the Autocart system (Arthrex, Naples, FL). The MFX group consisted of patients treated with MFX using the Steadman technique. Of the 41 studies, 7 were LOE I, 4 were LOE II, 11 were LOE III, and 19 were LOE IV. Additional characteristics of each individual study are presented in Table 3.

Quality Assessment

Of the 41 studies, 9 (22%) were RCT. Among the remaining studies, 5 (12%) were comparative, and 27 (66%) were noncomparative. Of the 32 non-RCT studies, the Methodological Index for Non-Randomized Studies assessment was performed and resulted in scores of 19.0 ± 1.4 in comparative studies and 10.6 ± 1.7 in noncomparative studies (Table 1). Of the 9 RCTs, all showed high risk of bias, associated primarily with high loss to follow-up (Table 2). Twenty studies clearly included consecutive patients. One study used blinded assessors to record relevant clinical outcomes. Two studies had loss to follow-up of less than 5%, and 20 did not report loss to follow-up. Eight studies conducted an a priori power analysis to ensure adequate study size. All 5 comparative studies showed baseline equivalence between cohorts, adequate control groups, and adequate statistical analysis. When applying the Risk of Bias 2.0 framework, all studies showed low risk in randomization, deviation from intended intervention, and outcome measurement, but consistent high risk in missing outcome data, primarily because of limited long-term follow-up. If loss to follow-up is disregarded, all trials would be classified as moderate risk overall, driven primarily by uncertainty in prespecified statistical analysis plans rather than evidence of selective or differential outcome reporting. Sex

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TABLE 2 Risk of Bias Assessment Using the Cochrane RoB2 Tool for Randomized Studies Included in This Review

Author and Year	1. Bias Arising From the Randomization Process	2. Bias Because of Deviations From Intended Intervention	3. Bias Because of Missing Outcome Data	4. Bias in the Measurement of the Outcome	5. Bias in Selection of the Reported Results	Total Score
Barié et al. 2020[44]	Low	Low	High	Low	Moderate	High
Brittberg et al. 2018[45]	Low	Low	High	Low	Moderate	High
Hoburg et al. 2022[46]	Low	Low	High	Low	Moderate	High
Ibarra et al. 2021[47]	Low	Low	High	Low	Moderate	High
Kim et al. 2020[48]	Low	Low	High	Low	Moderate	High
Kim et al. 2024[49]	Low	Low	High	Low	Moderate	High
Niemeyer et al. 2020[50]	Low	Low	High	Low	Low	High
Snow et al. 2023[51]	Low	Low	High	Low	Low	High
Yoon et al. 2024[52]	Low	Low	High	Low	Moderate	High

Note: Each Domain Represents a Specific Methodological Criterion, With Color Coding Indicating the Overall Judgment of Risk (Low = Low Risk, Moderate = Some Concerns, High = High Risk). All Studies Showed a High Overall Risk of Bias Primarily Because of Inadequate Follow-Up, Whereas Most Were Additionally Rated as Moderate Risk in Domains Related to Unclear Prespecification of Analysis Plans.
RoB2, Risk of Bias 2.0.

desegregation was not performed owing to the lack of reporting of outcomes based on sex.

Patient-Reported Outcome Measures

International Knee Documentation Committee

Postoperative IKDC scores were reported in 28 studies, with mean values ranging from 48.5 to 84.2 points (Figure 2).[8,9,15,16,18-21,28,29,31,33-36,38,39,41,43-52] By subgroup, mean scores ranged from 57.3 to 84.2 points for ACI, 48.5 to 81.6 points for MACI, 66.3 to 77.0 points for AMCI, and 50.7 to 71.2 points for MFX. Heterogeneity was $I^2 = 93\%$ for ACI, $I^2 = 87\%$ for MACI, $I^2 = 0\%$ for AMCI, and $I^2 = 68\%$ for MFX. Overall heterogeneity was $I^2 = 88\%$.

KOOS Activities of Daily Living

Postoperative KOOS Activities of Daily Living scores were reported in 17 studies, with mean values ranging from 18.0 to 94.1 points (Figure 3).[15,18,25-29,31,36-38,41,45-49] By subgroup, mean scores ranged from 21.5 to 86.3 points for ACI, 64.2 to 94.1 points for MACI, 80.9 to 87.8 points for AMCI, and 18.0 to 83.1 points for MFX. Heterogeneity was $I^2 = 98\%$ for ACI, $I^2 = 94\%$ for MACI, $I^2 = 15\%$ for AMCI, and $I^2 = 99\%$ for MFX. Overall heterogeneity was $I^2 = 99\%$.

KOOS Pain

Postoperative KOOS Pain scores were reported in 18 studies, with mean values ranging from 21.9 to 91.2 points (Figure 4).[9,15,18,25-29,31,36-38,41,45-49] By subgroup, mean scores ranged from 23.4 to 82.2 points for ACI, 50.0 to 91.2 points for MACI, 72.8 to 85.1 points for AMCI, and 21.9 to 77.9 points for MFX. Heterogeneity was $I^2 = 98\%$ for ACI, $I^2 = 96\%$ for MACI, $I^2 = 0\%$ for AMCI, and $I^2 = 98\%$ for MFX. Overall heterogeneity was $I^2 = 99\%$.

KOOS Quality of Life

Postoperative KOOS Quality of Life scores were reported in 19 studies, with mean values ranging from 32.1 to 80.4 points (Figure 5).[9,15,18,25-29,31,35-38,41,45-49] By subgroup, mean scores ranged from 40.4 to 74.2 points for ACI, 40.3 to 80.4 points for MACI, 48.4 to 66.3 points for AMCI, and 32.1 to 61.7 points for MFX. Heterogeneity was $I^2 = 94\%$ for ACI, $I^2 = 95\%$ for MACI, $I^2 = 59\%$ for AMCI, and $I^2 = 86\%$ for MFX. Overall heterogeneity was $I^2 = 93\%$.

KOOS Sports

Postoperative KOOS Sports scores were reported in 17 studies, with mean values ranging from 28.9 to 77.9 points (Figure 6).[9,15,18,25-29,31,36,38,41,45-49] By subgroup, mean scores ranged from 37.2 to 71.0 points for ACI,

TABLE 3 Individual Study Characteristics

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Akgun et al.[15]	II	Prospective, single-site, randomized, single-blind pilot study	MACI (Chondro-Gide)	7	4/3	32.7 ± 10.4 (18-46)	24	24.3 ± 0.8 (23.2-25.5)	3.0 ± 0.8 (2.3-4.3)	MFC: 5 LFC: 2	ICRS grade III-IV	KOOS Pain: 82.54 ± 3.48 KOOS Symptoms: 83.67 ± 2.81 KOOS ADL: 83.61 ± 2.61 KOOS Sport/Rec: 77.86 ± 3.93 KOOS QoL: 80.36 ± 5.62 VAS Frequency: 1.43 ± 0.53 VAS Severity: 1.14 ± 0.69 Tegner: 6.29 ± 0.49	None	Randomization by sealed envelope; blinded independent assessor; strict exclusion	Small cohort; single site; patient blinding incomplete
Andriolo et al.[16]	IV	Prospective case series	MACI (Hyalograft C)	41	25/16	42.6 ± 9.2	180 (168-216)	25.9 ± 2.7	4.0 ± 1.8	MFC: 27 LFC: 8 Patella: 3 Tibial plateau: 2 MFC + LFC: 1	ICRS grade III-IV	IKDC: 56.2 ± 21.7 EQ-VAS: 60.4 ± 17.5 Tegner: 2.7 ± 1.1	24 failures; 21 reoperation (2 scaffold implantation, 1 mosaicplasty, 18 prosthetic resurfacing)	Excluded KL > III OA, kissing lesions, >50% meniscectomy, untreated malalignment or instability; prospective follow-up	Heterogeneous cohort; no control group; high proportion of concomitant procedures
Barié et al.[44]	II	Prospective randomized controlled trial	1st-generation ACI	7	7/0	28.8 ± 9.1	103 ± 9.6	25.41 ± 2.55	4.08 ± 0.44	MFC: 7	Outerbridge grade III-IV	Tegner: 5.6 ± 2.1 Lysholm: 82 ± 17.2 IKDC: 81.6 ± 12.2 SF-36 Physical: 32 ± 0.7 SF-36 Mental: 13.6 ± 1	2 failures (synovectomy)	Randomized; strict exclusion (kissing lesions, KL > II OA, >1/3 meniscal resection, untreated ligamentous laxity, malalignment >5°, obesity, prior procedures <1 yr)	Small cohort; underpowered; limited generalizability; sex imbalance
Barié et al.[44]	II	Prospective randomized controlled trial	MACI (3rd-generation ACI, collagen membrane)	9	4/5	30.4 ± 6.8	115.2 ± 10.8	23.32 ± 1.15	4.27 ± 0.2	MFC: 8 LFC: 1	Outerbridge grade III-IV	Tegner: 4.9 ± 2.3 Lysholm: 72.4 ± 16.4 IKDC: 70.4 ± 19.3 SF-36 Physical: 31.5 ± 1.2 SF-36 Mental: 12.6 ± 1.3	3 failures (3 arthroscopic for symptomatic hypertrophy and 2 arthroscopy for pain and cartilage thinning)	Randomized; strict exclusion (kissing lesions, KL > II OA, >1/3 meniscal resection, untreated ligamentous laxity, malalignment >5°, obesity, prior procedures <1 yr)	Small cohort; underpowered; limited generalizability
Berruto et al.[19]	IV	Prospective single-center study	ACI (1st-generation n = 9, 2nd-generation n = 23)	32	22/10	31.61 ± 10.25	162 ± 27 (88-208)	NR	5.48 ± 1.53 (2-9)	MFC: 18 LFC: 2 PFT: 5 PFP: 6 Combined: 2 (1 MFC + patella, 1 LFC + patella)	Outerbridge grade III-IV	IKDC: 80.3 ± 14.2 EQ-VAS: 83 ± 11.4 Tegner: 4.8 ± 1.4	5 failures (1 TKA, 1 MFX, 3 clinical failures)	Excluded patients >50 yrs, OA, inflammatory arthritis, kissing lesions; subgroup analysis by age, sex, lesion size, location, cause, ACI generation	Small sample size, nonrandomized, no control group

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Binder et al.[20]	III	Retrospective cohort study, single center	MACI (Chondro-Gide, Hyalograft C, CaReS, NOVOCART 3D)	88	61/27	34 ± 10.03 (18-48)	24	25.2 ± 3.51	4.27 ± 1.7	MFC: 64 LFC: 21 MFC + LFC: 3	NR	Brittberg: 2 ± 0.8 IKDC: 73 ± 17.5 VAS: 2.0 ± 1.9 Tegner-Lysholm: 4.3 ± 1.2	None	Excluded knees with KL > II, instability, >50% meniscectomy, malalignment >5°, inflammatory disease, BMI > 30; only tibiofemoral lesions included; groups compared for age, sex, BMI, defect size	Retrospective; small subgroups per scaffold-type
Brittberg et al.[45]	I	Prospective randomized controlled multicenter trial	MACI (porcine collagen I/II membrane)	65	40/25	NR (18-54)	60	NR	5.1 ± 3.0	MFC: 48 LFC: 13 Trochlea: 4	Outerbridge grade III: 19 Outerbridge grade IV: 46	KOOS Pain: 82.2 ± 20.1 KOOS function: 61.9 ± 30.9 KOOS ADL: 86.4 ± 17.6 KOOS QoL: 59.8 ± 24.6 KOOS Symptoms: 80.9 ± 18.0 Cincinnati: 6.6 ± 2.1 IKDC: 68.5 ± 21.2 SF-12 Physical: −0.20 ± 0.95 SF-12 Mental: 0.41 ± 0.9 EQ-5D VAS: 80.4 ± 13.7	1 failure; 7 reoperations	Randomized allocation; exclusion of severe OA and major malalignment; stratified by site and lesion location	Extension study design with voluntary enrollment could introduce potential bias; not blinded
Bumberger et al.[21]	III	Retrospective registry-based matched-pair comparative study	Hydrogel-based ACI	45	27/18	37.4 ± 10.4 (18-68)	24	26.6 ± 4.2 (20-38.9)	5.4 ± 1.9 (4-12)	MFC: 22 LFC: 7 Patella: 8 Trochlea: 6 LTP: 2	ICRS grade III-IV	KOOS total: 79.8 ± 15.8 IKDC: 70.9 ± 18.0	NR	Propensity-score matched 1:1 by age, sex, BMI, previous surgeries, defect size/location, symptom duration; excluded OA > KL II, malalignment >3°, bipolar/kissing lesions, >1/3 meniscus resection	Retrospective registry design; exclusion of combined procedures may limit generalizability
Bumberger et al.[21]	III	Retrospective registry-based matched-pair comparative study	Spheroid-based MACI	45	23/22	35.3 ± 11.2 (16-57)	24	25.6 ± 4.3 (19.2-38.5)	5.5 ± 2.2 (4-16)	MFC: 27 LFC: 9 Patella: 9	ICRS grade III-IV	KOOS total: 73.3 ± 17.4 IKDC: 60.7 ± 20.2	NR	Propensity-score matched 1:1 by age, sex, BMI, previous surgeries, defect size/location, symptom duration; excluded OA > KL II, malalignment >3°, bipolar/kissing lesions, >1/3 meniscus resection	Retrospective registry design; exclusion of combined procedures may limit generalizability
Carey et al.[22]	IV	Retrospective case series	1st-generation ACI	55	33/22	26.1	217.35 (120-312)	NR	6 (0.9-12.3)	MFC: 43 LFC: 15 Trochlea: 1 Patella: 2	NR	KOOS Pain: 79.3 KOOS Symptoms: 60.2 KOOS ADL: 85.5 KOOS S/R: 53.9	29 reoperations (17 arthroscopy, 8 revision ACI, 2 osteotomy, 2 TKA)	Controlled for prior surgery, symptom duration, and concomitant procedures with no significant differences	Limited cohort size; considerable variation in duration of symptoms, prior

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TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
												KOOS QoL: 52.7 Tegner-Wallgren: 9.1 Lysholm: 75.4			surgery status, and defect location; no preoperative outcome scores; no comparator
Cvetanovich et al.[23]	IV	Retrospective case series	1st- and 2nd-generation ACI	37	15/22	16.7 ± 1.5	55.2 ± 28.8 (24-127.2)	22.8 ± 3.8	4.0 ± 2.2	MFC: 15 LFC: 8 Trochlea: 7 Patella: 7	Outerbridge grade IV	IKDC: 64.6 SF-12 Physical: 42.9 SF-12 Mental: 55.7 KOOS Pain: 78.2 KOOS Symptoms: 73.6 KOOS ADL: 87.9 KOOS Sports: 61.0 KOOS QoL: 55.3	35 reoperations (19 debridement, 4 meniscectomy, 3 MFX, 3 LBR, 2 meniscal repair, 2 lateral release, 1 MPFLr, 1 OCA)	Excluded patients with subchondral bone loss, OA, inflammatory arthritis; corrected malalignment/ligament insufficiency; subgroup analyses by lesion location, MAT, and subsequent surgery (no significant differences)	Small sample; heterogeneity in lesion location, prior procedures, demographics, and concomitant procedures; high rate of concomitant procedures
Dai et al.[24]	IV	Prospective case series	MACI	30	24/6	26 (12-48)	44 (6-60)	22.2 (16-30)	4.8 (2.0-20.0)	14 MFC, LFC 16, MFC + trochlea 1	ICRS IV	IKDC: 88.4 Lysholm: 95.9	4 reoperations (2 partial meniscectomy, 2 arthrolysis and debridement)	Excluded OA KL III-IV, multifocal/bilateral lesions, malalignment/instability, inflammatory disease	Small heterogeneous cohort; no control group; only limited second-look arthroscopies
Ebert et al.[26]	IV	Prospective case series	MACI	47	30/17	37.6 (20-61)	24	25.4 (19.5-33.8)	3.3 (1.0-7.2)	Patella: 24 Trochlea: 23	ICRS grade III-IV	KOOS Pain: 83.3 ± 11.4 KOOS Symptoms: 86.4 ± 9.8 KOOS ADL: 87.5 ± 11.0 KOOS Sport: 50.1 ± 29.4 KOOS QoL: 53.3 ± 23.0 SF-36 Physical: 47.1 ± 10.20 SF-36 Mental: 55.7 ± 6.1 VAS Frequency: 2.1 ± 1.4 VAS Severity 1.8 ± 1.1	2 graft failures; 3 complications (3 graft hypertrophy, 1 with DVT)	Excluded BMI > 35, malalignment >3°, ligamentous instability, inflammatory arthritis	No control group; relatively small sample
Ebert et al.[25]	IV	Prospective case series	Arthroscopic MACI	31	15/16	35.3 (16-57)	60	26.2 (18.4-34.8)	2.52 (1.0-5.0)	MFC: 18 LFC: 7	ICRS grade III-IV	KOOS Pain: 91.2 ± 1.8 KOOS	2 graft failures; 7 hypertrophic grafts	Strict exclusions (BMI > 35, KL > II OA, instability, extensive meniscectomy,	No control group; pilot cohort; small

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
										MTP: 2 LTP: 4		Symptoms: 85.6 ± 2.1 KOOS ADL: 94.1 ± 1.6 KOOS Sport: 71.5 ± 4.7 KOOS QoL: 67.5 ± 4.6 Lysholm: 86.8 ± 4.2 Tegner: 5.5 ± 0.5 SF-12 Physical: 51.0 ± 1.4 SF-12 Mental: 54.6 ± 1.4 VAS Frequency: 1.9 ± 0.4 VAS Severity: 1.7 ± 0.3 6 min walk: 640.9 ± 13.2 Knee flexion ROM: 143.5 ± 1.2 Knee extension ROM: −1.9 ± 0.3		inflammatory arthritis, malalignment >3°)	sample; single center
Gobbi et al.[27]	II	Prospective comparative	MACI (HYAFF 11 scaffold)	19	9/10	43.10 ± 5.81	59.69 (48.2-74.7)	24.31 ± 1.37	9.73 ± 6.09	Patella: 7 Trochlea: 5 Multiple: 7	ICRS grade IV	IKDC subjective: 75.70 ± 9.85 KOOS Pain: 80.73 ± 11.79 KOOS Symptoms: 81.05 ± 11.04 KOOS ADL: 82.15 ± 11.29 KOOS Sport/Rec: 68.84 ± 15.25 KOOS QoL: 76.10 ± 16.90 Tegner: 5.26 ± 1.14 VAS: 0.84 ± 0.68	1 reoperation (debridement)	Excluded tricompartmental OA, uncorrected malalignment, ligament insufficiency; compared baseline between groups with no significant differences; all by the same surgeon	Nonrandomized design; small sample size; midterm follow up only; only a subset underwent second-look and biopsy procedure
Heinz et al.[28]	IV	Retrospective registry-based case series	3rd-generation ACI (NOVOCART 3D)	51	33/18	32.67 ± 8.37	12	27.33 ± 5.61	3.43 ± 1.39	MFC: 21 LFC: 10 Trochlea: 3 Patella: 27 Tibial plateau: 2	NR	KOOS Symptoms: 54.11 ± 11.45 KOOS Pain: 76.06 ± 19.20 KOOS ADL: 82.11 ± 16.68	NR	Excluded inflammatory arthritis and ligament injury; registry-based standardized data collection; PROMs at defined intervals (preop, 6, 12 mo)	Retrospective design; small sample; monocentric subcohort from larger registry;

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
												KOOS Sport: 50.56 ± 23.94 KOOS QoL: 45.28 ± 19.03 IKDC: 59.83 ± 17.93 NRS: 2.63 ± 2.22			short follow-up; no control group
Hoburg et al.[46]	I	Prospective multicenter randomized controlled trial	ACI with spheroids	52	33/19	36 ± 10	60	25.7 ± 3.3 (18.8-31.2)	2.2 ± 0.7 (0.5-3.5)	Femur: 52	ICRS grade III: 17 ICRS grade IV: 31	KOOS total: 28.0 ± 18.4 KOOS Pain: 23.4 ± 22.3 KOOS Symptoms: 17.4 ± 20.0 KOOS ADL: 21.5 ± 18.3 KOOS Sport: 37.2 ± 31.4 KOOS QoL: 40.4 ± 20.3 IKDC Physical: 53.7 ± 7.7 IKDC Mental: 53.5 ± 7.9 IKDC subjective: 84.1 ± 14.3 Modified Lysholm: 22.5 ± 2.4	30 patients with 71 adverse events (24 joint effusions, 13 arthralgia, 11 joint swelling, 1 bone marrow edema, 3 contusions)	Central randomization; excluded bilateral defects, OA, instability	Noninferiority design; no blinding of subjects; LOCF used
Ibarra et al.[47]	I	Prospective randomized controlled trial	Arthroscopic MACI (polyglycotic acid scaffold)	24	17/7	33.7 ± 9.4	74.0 ± 10.4	25.5 ± 3.1	1.9 ± 0.9	MFC: 7 LFC: 9 Trochlea: 1 Patella: 7	ICRS grade IV	Lysholm: 85.9 ± 19.8 Tegner: 6.5 ± 2.0 IKDC: 75.8 ± 19.2 KOOS Symptoms: 82.7 ± 19.8 KOOS Pain: 86.4 ± 20.4 KOOS ADL: 89.9 ± 15.9 KOOS Sports: 73.9 ± 27.8 KOOS QoL: 69.8 ± 23.2	34 adverse events (13 joint pain, 14 atrophy, 6 crepitation, 1 synovitis)	Randomization with minimization; strict inclusion criteria (18-50 y, 1-4 cm^2, ICRS III-IV, BMI < 30, no KL ≥ III, no untreated instability or major malalignment)	Small sample; high number of concomitant procedures
Kreuz et al.[29]	IV	Prospective case series	MACI (BioSeed-C polymer-based scaffold)	21	8/13	45.35 (29-63)	141 (122-157)	26.08 (18.59-37.14)	4.34 (1.5-9.6)	Femoral condyle: 12 Retropatellar: 6 Trochlea: 3	ICRS grade IV	IKDC: 71.15 ± 16.56 Lysholm: 86 KOOS Pain: 84.0 ± 12.88 KOOS ADL: 93.0 ± 9.47 KOOS Sport/Rec:	NR	Excluded malalignment >5°, KL > III, inflammatory arthritis; clinical outcomes assessed by blinded observers	Small follow up cohort; heterogeneity in defect sites and concomitant procedures; registry attrition bias

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
												56.0 ± 26.26 KOOS QoL: 58.0 ± 21.45 KOOS Symptoms: 72.0 ± 16.69 Noyes: 75			
Matsushita et al.[30]	IV	Phase I/IIa open-label clinical trial	3rd-generation ACI (CaReS)	7	4/3	38.9 ± 8.6	12	NR	4.1 ± 0.9 (2.0-4.5)	MFC: 4 LFC: 1 Trochlea: 1 Patella: 1	ICRS III: 2 ICRS IV: 5	IKDC: 74.1 Lysholm: 89.6 VAS: 22.9	62 adverse events (18 wound complications, 6 joint effusions, 1 delayed wound healing, 1 MRSA + septic arthritis)	Required stable surrounding cartilage; excluded OA, kissing lesions, recent meniscus/ligament surgery	Small sample size; no control group; 1-year follow-up
Mayr et al.[31]	III	Retrospective controlled cohort study	MACI	10	7/2	43.4 ± 5.7 (37-53)	25.3 ± 1.2 (24-27)	NR	> 6	MFC: 4 LFC: 1 Trochlea: 5	ICRS grade IV	VAS: 6.1 ± 3.5 Tegner: 2.9 ± 1.4 IKDC: 48.5 ± 23.1 KOOS Pain: 50.0 ± 22.7 KOOS Symptoms: 46.1 ± 16.5 KOOS ADL: 64.2 ± 24.6 KOOS Sports: 28.9 ± 17.8 KOOS QoL: 40.3 ± 34.8	NR	Strict exclusions (OA, bifocal lesions >Grade II, malalignment >3°, ligamentous instability, subtotal meniscectomy, inflammatory disease); all first-line procedures; MRI and PROMs assessed by 2 independent surgeons	Small cohort; retrospective design
Niemeyer et al.[50]	I	Prospective, single-blind, randomized controlled trial	Matrix-associated ACI with spheroids	75	53/22	34 ± 9	48	25.2 ± 3.1 (19.0-33.2)	5.6 ± 1.6 (2-10)	Femur: 28 Patella: 47	ICRS grade III-IV	KOOS total: 77.1 ± 18.6 IKDC: 74.6 ± 18.7	3 failures requiring reoperation (1 cartilage hypertrophy, 1 osteochondrosis/osteonecrosis, 1 extraskeletal ossification); 126 adverse events in 63 patients	Randomized by defect size; blinded radiologist for MRI; patients blinded to dose group	Tibial defects not included; some dose misallocations because of inadequate cell proliferation
Niemeyer et al.[32]	III	Propensity-matched cohort study	MACI (NOVOCART inject plus)	72	51/21	39.3 ± 12.1 (15-62)	24	27.1 ± 4.1 (20.4-34.4)	6.4 ± 2.1 (4.0-12.5)	Femur: 82 Patella: 10 Tibia: 4	ICRS grade III: 72 ICRS grade IV: 24	KOOS: 81.81 ± 16.772 IKDC: 75.4	6 reoperations; 1 complication (lateral patellar compression syndrome)	Propensity score matching for age, sex, prior knee surgery, baseline KOOS, symptom duration; excluded prior failed cartilage repair	Propensity matching limited variables (imbalances in defect size, location, cause, # defects); historical comparator; industry-sponsored

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Niethammer et al.[33]	III	Retrospective comparative study	Hydrogel-based ACI (NOVOCART Inject)	25	13/12	37 ± 12.8	24	27.2 (18.7-39.1)	4.4 ± 3.1 (1.0-12.0)	MFC: 12 LFC: 1 Patella: 11 Trochlea: 1	ICRS grade III-IV	IKDC: 66.7 ± 21.7 VAS: 2.0 ± 2.3	NR	Matched for sex, number of defects, localization; excluded malalignment >3-5°, KL > II OA, subtotally resected meniscus, RA with synovitis, hemophilia arthropathy, bipolar defects	Small cohort; possible learning curve with hydrogel ACI
Niethammer et al.[33]	III	Retrospective comparative study	Scaffold-based ACI (NOVOCART 3D)	25	13/12	33.9 ± 11.6	24	26.3 (20.9-35.3)	5.5 ± 2.8 (0.8-12.0)	MFC: 9 LFC: 3 Patella: 12 Trochlea: 1	ICRS grade III-V	IKDC: 67.8 ± 18.4 VAS: 2.0 ± 2.1	NR	Matched for sex, number of defects, localization; excluded malalignment >3°-5°, KL > II OA, subtotally resected meniscus, RA with synovitis, hemophilia arthropathy, bipolar defects	Small cohort; possible learning curve with hydrogel ACI
Retzky et al.[35]	IV	Retrospective case series	MACI (Vericel membrane)	30	7/23	NR (median = 35.1)	32.4 ± 18 (13.2-68.4)	NR (median = 23.6)	3.1 ± 0.75	Patella: 27 Trochlea: 3	Outerbridge grade IV	IKDC: 61.8 ± 18.4 KOOS QoL: 46.5 ± 23.0 Kujala: 72.4 ± 15.9	2 reoperation (PF arthroplasty)	Excluded partial-thickness lesions, tibiofemoral OA, kissing lesions; all procedures by one surgeon	Small sample; retrospective design
Rosa et al.[36]	IV	Retrospective case series	1st-generation ACI	15	9/6	21.33 ± 8.92	148.1 ± 15.76 (125-177)	NR	5.08 ± 2.01 (2-9)	MFC: 10 LFC: 2 Patella: 2 Tibial plateau: 1	Outerbridge grade III-IV ICRS grade II-III for OCD lesions	IKDC: 76.32 ± 32.36 Tegner activity: 4.93 ± 2.43 KOOS Pain: 79.63 ± 33.33 KOOS Symptoms: 76.42 ± 32.47 KOOS ADL: 85.09 ± 34.62 KOOS Sport: 70.33 ± 31.13 KOOS QoL: 74.17 ± 32.72	2 failures (graft removal and MFX); 4 graft hypertrophy	Excluded age >45, OA (KL ≥ II), BMI > 35, kissing lesions, inflammatory arthritis/infection, malalignment >5°, untreated instability	Lack of control group; retrospective design; limited comparability because of small sample size
Schneider et al.[37]	III	Retrospective matched-pair comparative study	MACI (hydrogel based)	16	15/1	36.9 ± 7.9	24	26.7 ± 3.3	2.5 ± 1.2	MFC: 6 LFC: 3 MFC + LFC: 2 Trochlear: 3 Retropatellar: 2	Grade III: 3Grade III-IV: 4 Grade IV: 9	VAS: 2.1 ± 1.7 KOOS Pain: 80.56 ± 13.08 KOOS Symptoms: 74.60 ± 14.30 KOOS ADL: 86.64 ± 11.79 KOOS QoL: 49.48 ± 16.74 Tegner activity: 3.63 ± 1.51	2 reoperations/ adverse event (persistent pain)	Matched for age, sex, BMI, lesion size/location; excluded combined procedures	Retrospective design; small sample; limited power; female underrepresented

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Siebold et al.[38]	IV	Prospective case series	Arthroscopic ACI with spheroids	30	19/11	35.5 ± 9.5	34.8 ± 10.2 (24-62)	23.8 ± 2.8 (19-29)	6.0 ± 3.1 (1.5-16)	MFC: 12 LFC: 6 Patella: 7 Trochlea: 5	NR	KOOS Pain: 82.2 ± 16.1 KOOS Symptoms: 81.7 ± 12.1 KOOS ADL: 86.3 ± 15.6 KOOS Sports: 71.0 ± 16.0 KOOS QoL: 72.3 ± 16.9 Lysholm: 77.7 ± 14.6 Tegner: 5 IKDC: 84.2 ± 5.6	3 failures (MOCART of 0)	Excluded malalignment >3°, ligament instability, additional cartilage damage, prior ipsi/contralateral knee surgery, BMI > 30, OA, inflammatory arthritis	Small cohort; midterm follow-up; no control group; influence of cause not analyzed
Snow et al.[51]	I	Randomized controlled trial	ACI (periosteum, collagen, matrix, chondron)	195	125/70	35.4 ± 9.2	60	NR	3.2 ± 2.1	Femoral: 171 Trochlear/patella: 24	ICRS grade III-IV	Lysholm: 64.78 ± 25.53 IKDC: 57.3 ± 24.9 EQ-5D-3L: 0.67 ± 0.33	33 adverse events	Central randomization with minimization; blinded independent assessors	Underpowered for cessation-of-benefit endpoint; pragmatic design with varied ACI and comparator techniques
Uchio et al.[40]	IV	Retrospective multicenter case series	Periosteum-covered MACI	232	126/106	40.9 ± 15.0 (12-74)	24	24.0 ± 3.9	5.6 ± 2.4	MFC: 132 LFC: 44 Patella: 25 Trochlea: 86 Tibial plateau: 4	NR	Lysholm: 87.5 KOOS total: 75.2 KOOS Symptoms: 80.4 KOOS Pain: 84.6 KOOS ADL: 88.8 KOOS Sport/Rec: 60.5 KOOS: QoL: 61.9	86 adverse events; 26 reoperations (arthroscopic debridement)	Excluded OA, autoimmune disease, hypersensitivity to culture reagents; mandatory nationwide registry; uniform surveillance protocol	No control group; multiple concomitant procedures; heterogeneity of sites and pathologies
van Duijvenbode et al.[41]	IV	Retrospective case series	Gel-type ACI (GACI) with fibrin scaffold after ACLR	19	10/9	35 ± 8	24	24 (22-33)	9 ± 4 (2-17)	MFC: 6 MFC + trochlea: 5 MFC + LFC + trochlea: 1 LFC: 3 LFC + patella: 1 LFC + trochlea: 2 Trochlea + patella: 1	ICRS grade III-IV	IKDC: 59 ± 18 KOOS Pain: 72 ± 21 KOOS Symptoms: 72 ± 16 KOOS ADL: 79 ± 19 KOOS Sports: 46 ± 28 KOOS QoL: 49 ± 22	7 reoperations (1 GACI, 3 arthroscopic debridement, 2 MFX, 1 PF arthroplasty)	Required stable ACLR ≥12 mo before GACI; excluded unstable knees or new injuries; subgroup analyses by lesion number and surgical history	Retrospective design; absence of control group; small cohort
Weishorn et al.[42]	IV	Prospective case series	MACI (NOVOCART 3D)	103	53/50	29.3 (18-51)	97.2 (60-142.8)	26.4 (18-42)	4.8 (1.2-12)	Femorotibial: 68 Patellofemoral: 35	ICRS grade III: 7 ICRS grade IV: 96	KOOS total: 70.0 KOOS Symptoms: 56.5 KOOS Pain: 80.5 KOOS ADL: 87.3 KOOS Sports: 62.8 KOOS QoL: 63.1 EQ-5D: 81.7 VAS: 2.8	2 failures; 3 reoperations (1 MFX, 2 arthroplasty)	Excluded KL > II, ligamentous instability, varus/valgus deformity >5°, inflammatory arthritis, hemophilia, bipolar/kissing lesions, subtotal meniscal loss	Single-center; limited power for subgroup analysis

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Yoon et al.[43]	III	Retrospective comparative trial	1st-generation ACI	14	11/3	31.2 ± 9.9	13.1 ± 2.4	25.1 ± 3.3	3.0 ± 1.5	MFC: 7 LFC: 7	ICRS grade IV	IKDC: 75.8 ± 18.4 Lysholm: 77.5 ± 19.1 Tegner: 5.3 ± 1.1	4 failures	Excluded revision ACI, PF lesions, malalignment >3°, HTO/DFO, bilateral knees, osteotomy in other compartment, follow-up <10 yrs	Retrospective design; small sample size
Yoon et al.[52]	II	Prospective clinical trial	Costal chondrocyte-derived pellet-type ACI	16	13/3	39.4 ± 13.4	60	24.3 ± 2.5	3.6 ± 1.4	Condyle: 5 Trochlea: 11	ICRS grade III-IV	Lysholm: 84.5 ± 13.0 IKDC: 64.4 ± 15.9 KOOS: 390.9 ± 69.9 VAS pain: 18.3 ± 19.7	None	RCT design; strict inclusion	Small sample; single-center; exploratory phase 2 trial
Barbaret et al.[17]	III	Retrospective multicentric case series	Autologous minced cartilage (autocart) with PRP	66	52/14	30.4 ± 11.2	20.5 ± 7.5 (12-36.8)	23.8 ± 3.5	2.6 ± 1.3	Femoral-patellar: 30 Internal: 18 External: 18	ICRS grade III: 52 ICRS grade IV: 14	KOOS total: 71.5 KOOS Pain: 80.4 KOOS Symptoms: 79 KOOS ADL: 85.3 KOOS Sports: 74.8 KOOS QoL: 73.7 IKDC: 73.7 SKV: 81.2	2 reoperations (2 debridement)	Excluded patients with follow up < 1 year and Ahlbäck <2 OA; MRI scored by 2 independent surgeons	Short-term follow-up; no comparative group
Behrendt et al.[18]	III	Matched-pair, retrospective, comparative cohort study	Autologous minced cartilage with fibrin glue	24	13/11	29.2 ± 14.1 (14-58)	32.2 ± 7.9 (24-48)	NR	2.6 ± 1.5	PF: 13 MFC: 8 LFC: 3	ICRS grade IV: 6 ICRS grade IV-a: 13 ICRS grade IV-b: 3	VAS: 4.1 ± 2.7 Lysholm: 70.1 ± 25.7 KOOS Pain: 72.8 ± 26.5 KOOS Symptoms: 77.2 ± 21.4 KOOS ADL: 82.6 ± 22.9 KOOS Sports: 60.4 ± 28.5 KOOS QoL: 50.4 ± 22.3	None	Matched design, multicenter	Retrospective design; small sample
Mayr et al.[31]	III	Retrospective controlled cohort study	Autologous minced cartilage (autocart) with PRP	10	5/5	41.1 ± 9.4 (28-54)	24.9 ± 1.0 (24-27)	NR	>6	MFC: 5 LFC: 1 Patella: 3 Trochlea: 1	ICRS grade IV	VAS: 0.6 ± 0.8 Tegner: 5.8 ± 1.5 IKDC: 77.0 ± 16.6 KOOS Pain: 82.3 ± 14.7 KOOS Symptoms: 72.9 ± 16.1 KOOS ADL: 80.9 ± 12.1 KOOS Sports: 67.0 ± 22.5 KOOS QoL: 66.3 ± 20.24	NR	Strict exclusions (OA, bifocal lesions >Grade II, malalignment >3°, ligamentous instability, subtotal meniscectomy, inflammatory disease); all first-line procedures; MRI and PROMs assessed by 2 independent surgeons	Small cohort; retrospective design

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Runer et al.[8]	III	Retrospective cohort study	Autologous minced cartilage with fibrin glue	28	15/13	29.5 ± 11.4	65.5 ± 4.1	24.4 ± 3.5	3.5 ± 1.8	Retropatellar: 19 MFC: 5 LFC: 5 MFC + LFC: 1 MFC + retropatellar: 1 LFC + retropatellar: 1 Trochlea: 1 Tibial: 1	ICRS grade III: 19 ICRS grade IV: 12	NAS Pain: 2 NAS Function: 3 Lysholm: 76.5 ± 12.5 IKDC: 71.6 ± 14.8 COMI: 2.2 ± 1.9 Tegner activity score: 4	4 complications (1 revision); 5 adverse events; 1 traumatic accident	Included only patients without need for subchondral bone treatment; single surgeon; consecutive enrollment	No comparative control; heterogeneity of defect locations and concomitant procedures; small sample size
Schneider et al.[7]	IV	Prospective case series	Autologous minced cartilage (autocart) with PRP	62	34/28	38.79 ± 10.78 (14-61)	24	26.95 ± 5.15 (19.0-43.8)	2.53 ± 1.24 (0.25-6.0)	MFC: 23 LFC: 13 Trochlea: 8 Patella: 12 Tibia: 1 Combined: 5	ICRS Grade III: 60 ICRS Grade IV: 2	VAS pain: 2.50 ± 2.26 WOMAC pain: 83.6 ± 18.3 WOMAC stiffness: 74.6 ± 26.1 WOMAC function: 84.6 ± 17.4 SANE: 67.1 ± 23.2 Tegner: 3.84 ± 1.69 KOOS total: 74.4 ± 15.9	5 revisions (4 hypertrophy resection, 1 implantation of mini-endoprosthesis)	Excluded kissing lesions, advanced OA, osteotomies; MRI and PROMs evaluated by independent blinded examiners	No control/comparator; single-arm case series; high rate of concomitant procedures may confound PROMs
Schneider et al.[37]	III	Retrospective matched-pair comparative study	Autologous minced cartilage (autocart) with PRP	16	15/1	36.7 ± 9.1	24	27.3 ± 4.5	2.6 ± 1.1	MFC: 7 LFC: 3 MFC + LFC: 2 Trochlear: 3 Retropatellar: 1	Grade III: 2 Grade III-IV: 3 Grade IV: 11	VAS: 2.0 ± 1.6 KOOS Pain: 83.89 ± 12.91 KOOS Symptoms: 83.97 ± 11.05 KOOS ADL: 87.75 ± 12.96 KOOS QoL: 61.25 ± 18.63 Tegner activity: 3.69 ± 2.02	3 adverse events (2 persistent pain, 1 ligament rupture)	Matched for age, sex, BMI, lesion size/location; excluded combined procedures	Retrospective design; small sample; limited power; female underrepresented
Wodzig et al.[9]	IV	Retrospective case series	Autologous minced cartilage with fibrin glue	18	13/5	23.0 ± 7.5	14.1 ± 2.7	22.8 ± 2.6	3.3 ± 2.1 (0.24-7.8)	MFC: 8 LFC: 6 Patella: 4	ICRS grade III: 2 ICRS grade IV-a: 3 ICRS grade IV-b: 13	VAS pain: 14 IKDC: 66.3 ± 20.2 KOOS total: 72.4 ± 15.6 KOOS Symptoms: 80.4 ± 12.5 KOOS pain: 85.1 ± 12.8 KOOS ADL: 94.0 KOOS sports: 57.1 ± 36.8 KOOS QoL: 48.4 ± 23.9 EQ-5D: 0.843 ± 0.128	2 reoperations (1 hardware removal, 1 arthroscopy for hypertrophic overgrowth); 1 adverse event	Included only patients with 12-mo MRI; excluded refixable OCD; registry-based prospective PROM collection; blinded radiology assessment	Short follow up, heterogeneity of patients/defects; multiple concomitant procedures; young cohort only

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Brittberg et al.[45]	I	Prospective randomized controlled multicenter trial	MFX	63	42/21	NR (18-54)	60	NR	4.9 ± 2.0	MFC: 44 LFC: 15 Trochlea: 4	Outerbridge grade III: 12 Outerbridge grade IV: 51	KOOS Pain: 74.8 ± 21.7 KOOS function: 50.3 ± 32.3 KOOS ADL: 80.0 ± 21.2 KOOS QoL: 52.4 ± 26.6 KOOS Symptoms: 74.8 ± 18.5 Cincinnati: 5.8 ± 2.2 IKDC: 61.8 ± 21.5 SF-12 Physical: −0.67 ± 1.1 SF-12 Mental: 0.46 ± 1.0 EQ-5D VAS: 73.8 ± 19.1	1 failure; 6 reoperations	Randomized allocation; exclusion of severe OA and major malalignment; stratified by site and lesion location	Extension study design with voluntary enrollment could introduce potential bias; not blinded
Hoburg et al.[46]	I	Prospective comparative	MFX	50	28/22	37 ± 9	60	25.8 ± 3.0 (18.2-30.0)	2.0 ± 0.8 (0.8-4.0)	Femur: 49 Femur and patella: 1	ICRS grade III: 20	Overall KOOS: 23.7 ± 19.9 KOOS Pain: 21.9 ± 20.4 KOOS Symptoms: 16.1 ± 21.3 KOOS ADL: 18.0 ± 18.5 KOOS Sports: 30.1 ± 28.6 KOOS QoL: 32.1 ± 27.1 IKDC Physical: 47.3 ± 10.1 IKDC Mental: 54.0 ± 8.3 IKDC subjective: 69.5 ± 19.7 Modified Lysholm: 20.8 ± 3.7	30 patients with 75 adverse events (18 joint effusion, 24 arthralgia, 10 joint swelling, 5 bone-marrow edema, 1 contusion)	Central randomization; excluded bilateral defects, OA, instability	Noninferiority design; no blinding of subjects; LOCF used
Ibarra et al.[47]	I	Prospective randomized controlled trial	MFX	24	14/10	35.8 ± 9.1	71.0 ± 15.6	26.6 ± 3.1	1.7 ± 0.7	MFC: 9 LFC: 6 Trochlea: 6 Patella: 3	ICRS grade IV	Lysholm: 78.8 ± 21.5 Tegner: 4.4 ± 2.3 IKDC: 66.6 ± 21.1 KOOS Symptoms: 81.8 ± 18.0 KOOS Pain: 77.9 ± 21.3	2 failures (1 revision MFX, 1 tissue repair); 17 joint pain, 12 atrophy, 4 crepitation, 1 septic arthritis	Randomization with minimization; strict inclusion criteria (18-50 y, 1-4 cm^2, ICRS III-IV, BMI < 30, no KL ≥ III, no untreated instability or major malalignment)	Small sample; high number of concomitant procedures

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
												KOOS ADL: 81.7 ± 20.1 KOOS Sports: 60.0 ± 34.6 KOOS QoL: 55.5 ± 30.3			
Kim et al.[48]	I	Multicenter prospective randomized controlled trial	MFX	44	9/35	51.75 ± 8.10 (24-63)	24	24.96 ± 3.65 (18.03-37.22)	4.67 ± 2.54 (1.13-12.75)	NR	ICRS grade III: 11 ICRS grade IV: 33	VAS Pain: 21.5 ± 25.9 KOOS Pain: 77.8 ± 16.1 KOOS Symptoms: 72.0 ± 17.3 KOOS ADL: 83.1 ± 14.7 KOOS Sport: 56.0 ± 25.2 KOOS QoL: 61.7 ± 22.3 KOOS total: 75.2 ± 15.5 IKDC Pain: 82.7 ± 25.1 IKDC Sport/Rec: 63.6 ± 18.5 IKDC ADL: 72.5 ± 24.4 IKDC total: 71.2 ± 19.9	2 severe adverse events (1 hospitalization for left knee pain and swelling, 1 hardware removal)	Randomization with block allocation; multicenter design; baseline demographics and defect characteristics not significantly different between groups	Korean-only cohort; ~50% HTO rate confounds results; single-blinded; not powered for subgroup analyses
Kim et al.[49]	I	Multicenter randomized controlled trial	MFX	14	2/12	55.07 ± 7.37 (42-66)	72	25.45 ± 4.08 (21.9-37.2)	5.03 ± 3.44 cm^2	MFC: 14	ICRS grade III: 5 ICRS grade IV: 9	VAS Pain: 20.01 ± 21.69 KOOS Pain: 76.59 ± 13.90 KOOS Symptoms: 69.39 ± 17.31 KOOS ADL: 82.46 ± 13.17 KOOS Sports: 50.36 ± 27.77 KOOS QoL: 58.93 ± 17.63 KOOS total: 67.54 ± 14.77 IKDC Pain: 52.90 ± 13.48 IKDC Health Status: 73.00 ± 15.88 IKDC Sport/Rec: 58.39 ± 17.83 IKDC ADL: 70.71 ± 19.00 IKDC total: 57.47 ± 11.49	None	Randomized with block method; strict inclusion/exclusion (isolated MFC defect, neutral or corrected alignment, no ligament surgery history)	Small sample; sex imbalance; single-blinded; potential type II error

TABLE 3 (Continued)

Study	LOE	Study Design	Technique	Patients in Study Group, n	Sex (M/F)	Age Mean ± SD (Range), Yr	Mean Follow-Up ± SD (Range), Mo	BMI Mean ± SD	Defect Size (cm^2)	Defect Location	Defect Grade	Mean PROMs at the Final Follow-Up	Failure Reoperation Adverse Events	Attempts to Reduce Potential Confounding Variables	Study Limitations
Niemeyer et al.[32]	III	Propensity-matched cohort study	MFX	72	51/21	39.3 ± 11.9 (18-61)	24	27.4 ± 3.9 (20.1-34.9)	3.7 ± 1.3 (2.0-6.0)	Femur: 79	ICRS grade III: 41 ICRS grade IV: 38	KOOS: 73.03 ± 20.628 IKDC: 68.8	3 reoperations	Propensity score matching for age, sex, prior knee surgery, baseline KOOS, symptom duration; excluded prior failed cartilage repair	Propensity matching limited variables (imbalances in defect size, location, cause, no. of defects); historical comparator; industry-sponsored
Pellegrino et al.[34]	IV	Retrospective case series	MFX	15	12/3	44.4	132	NR	NR	NR	Outerbridge grade III-IV	Lysholm: 82.13 ± 14.16 IKDC: 68.66 ± 21.47	NR	Strict exclusions (ligament reconstruction, meniscectomy, arthritis, malalignment, high BMI, skeletal immaturity) to isolate MFX outcomes	Small cohort; heterogeneous ages
Silva et al.[39]	III	Retrospective comparative case series	MFX	11	7/4	49.6 (39-55)	24	NR	NR	MFC: 10 Trochlear: 1	ICRS grade III-IV	SF-36 Physical: 73.6 ± 23.1 SF-36 Mental: 61.4 ± 23.4 Total IKDC: 68.5 ± 6.9 IKDC Symptoms: 68.5 ± 6.9 IKDC Sports: 31.1 ± 4.3 IKDC functional ADL: 5.9 ± 1.8 VAS: 4.5 ± 1.4	3 reoperations (1 arthroscopic debridement, 2 TKA)	Age/sex-matched controls; excluded ligament and meniscal injury, arthritis, prior invasive surgery; same surgeon/center	Small sample; single center/surgeon; limited generalizability
Yoon et al.[52]	II	Prospective clinical trial	MFX	9	3/6	47.0 ± 11.5	60	24.7 ± 2.1	2.4 ± 0.3	Condyle: 6 Trochlea: 3	ICRS grade III-V	Lysholm: 64.9 ± 26.4 IKDC: 50.7 ± 20.0 KOOS: 303.0 ± 101.1 VAS pain: 36.2 ± 28.0	1 failure (HTO)	RCT design; strict inclusion	Small sample; single-center; exploratory phase 2 trial

ACI, autologous chondrocyte implantation; ACLR, anterior cruciate ligament reconstruction; ADL, Activities of Daily Living; AMCI, autologous minced cartilage implantation; BMI, body mass index; CaReS, Cartilage Regeneration System; COMI, Core Outcome Measures Index; DFO, distal femoral osteotomy; DVT, deep vein thrombosis; EQ-5D, EuroQol 5-Dimension health index; EQ-5D-3L, EuroQol 5-Dimension 3-level version; EQ-VAS, EuroQol Visual Analog Scale; F, female; GACI, gel-type autologous chondrocyte implantation; HTO, high tibial osteotomy; HYAFF, hyaluronic acid-based scaffold; ICRS, International Cartilage Repair Society; IKDC, International Knee Documentation Committee; KL, Kellgren-Lawrence; KOOS, Knee injury and Osteoarthritis Outcome Score; LBR, loose body removal; LFC, lateral femoral condyle; LOCF, last observation carried forward; LOE, level of evidence; LTP, lateral tibial plateau; M, male; MACI, matrix-associated autologous chondrocyte implantation; MAT, meniscal allograft transplantation; MFC, medial femoral condyle; MFX, microfracture; Mo, month; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue; MPFLr, medial patellofemoral ligament reconstruction; MRI, magnetic resonance imaging; MRSA methicillin-resistant *Staphylococcus aureus*; MTP, medial tibial plateau; NAS, numeric analog scale; NR, not reported; NRS, numeric rating scale; OA, osteoarthritis; OCA, osteochondral allograft; OCD, osteochondritis dissecans; PF, patellofemoral; PFP, patellofemoral; PFT, patellofemoral trochlea; PROMs, patient-reported outcome measures; PRP, platelet-rich plasma; QoL, Quality of Life; RA, rheumatoid arthritis; RCT, randomized controlled trial; ROM, range of motion; S/R, sports and recreation; SANE, Single Assessment Numeric Evaluation; SD, standard deviation; SF-12, 12-Item Short Form Health Survey; SF-36, 36-Item Short Form Health Survey; SKV, Subjective Knee Value; TKA, total knee arthroplasty; VAS, Visual Analog Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; Yr, year.

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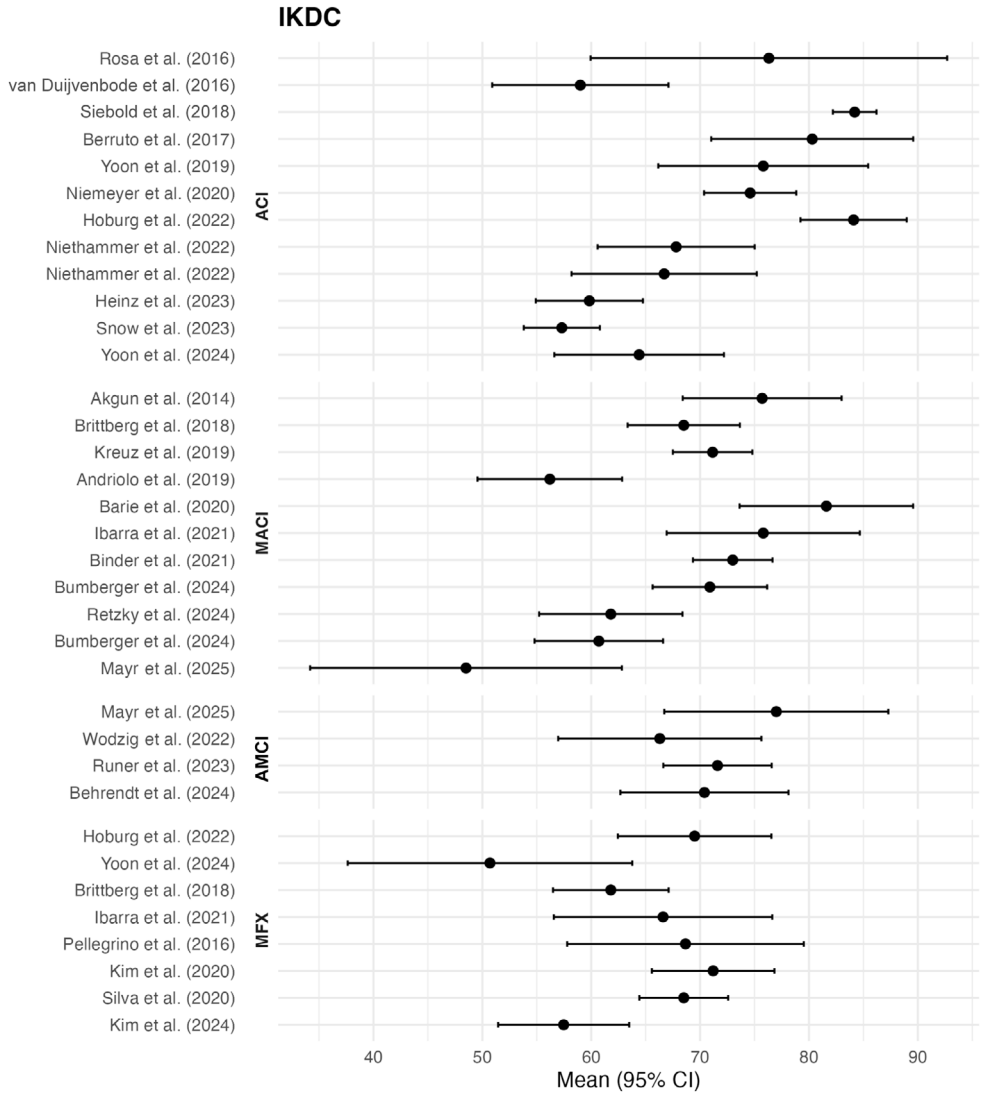

FIGURE 2 Forest plot illustrating postoperative IKDC scores with 95% CIs. Each horizontal line represents 1 study's mean postoperative IKDC score with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were intentionally omitted given substantial clinical heterogeneity across studies (overall I^2 = 88%). Overlapping CIs across treatment groups suggest comparable postoperative IKDC outcomes at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; AMCI, autologous minced cartilage implantation; CI, confidence interval; IKDC, International Knee Documentation Committee; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture.)

28.9 to 77.9 points for MACI, 57.1 to 67.0 points for AMCI, and 30.1 to 60.0 points for MFX. Heterogeneity was $I^2 = 91\%$ for ACI, $I^2 = 98\%$ for MACI, $I^2 = 0\%$ for AMCI, and $I^2 = 79\%$ for MFX. Overall heterogeneity was $I^2 = 94\%$.

KOOS Symptoms

Postoperative KOOS Symptoms scores were reported in 18 studies, with mean values ranging from 16.1 to 86.4 points (Figure 7).[9,15,18,25-29,31,36-38,41,45-49] By subgroup, mean scores ranged from 17.4 to 81.7 points for ACI, 46.1 to 86.4 points for MACI, 72.9 to 84.0 points for AMCI, and 16.1 to 81.8 points for MFX. Heterogeneity was $I^2 = 99\%$ for ACI, $I^2 = 98\%$ for MACI, $I^2 = 30\%$ for AMCI, and $I^2 = 98\%$ for MFX. Overall heterogeneity was $I^2 = 99\%$.

Lysholm

Postoperative Lysholm scores were reported in 10 studies, with mean values ranging from 64.8 to 86.8 points.[8,18,25,34,38,43,44,47,51,52] By subgroup, mean scores ranged from 64.8 to 84.5 points for ACI, 72.4 to 86.8 points for MACI, 70.1 to 76.5 points for AMCI, and 64.9 to 82.1

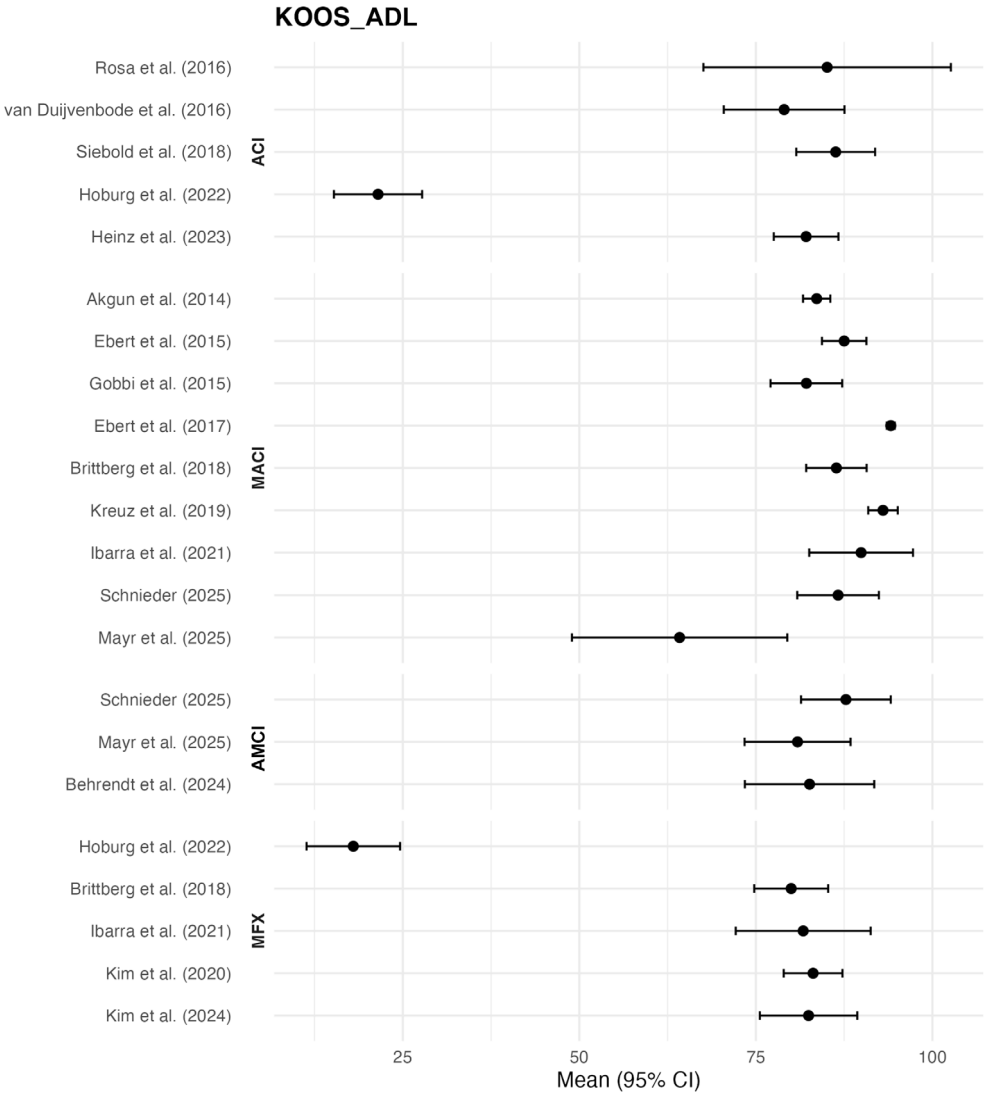

FIGURE 3 Forest plot illustrating postoperative KOOS ADL subscores with 95% CIs. Each horizontal line represents 1 study's mean postoperative KOOS ADL subscore with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were omitted given substantial heterogeneity (overall I^2 = 99%). Overlapping CIs across groups suggest comparable postoperative function in ADL at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; ADL, Activities of Daily Living; AMCI, autologous minced cartilage implantation; CI, confidence interval; KOOS, Knee Injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture.)

points for MFX. Heterogeneity was $I^2 = 85\%$ for ACI, $I^2 = 74\%$ for MACI, $I^2 = 22\%$ for AMCI, and $I2 = 23\%$ for MFX. Overall heterogeneity was $I^2 = 85\%$.

Tegner

Postoperative Tegner scores were reported in 13 studies, with mean values ranging from 2.7 to 6.5 points.[7,15,16,19,20,25,27,31,36,37,43,44,47] By subgroup, mean scores ranged from 4.8 to 5.6 points for ACI, 2.7 to 6.5 points for MACI, 3.7 to 5.8 points for AMCI, and 4.4 to 4.4 points for MFX. Heterogeneity was $I^2 = 0\%$ for ACI, $I^2 = 98\%$ for MACI, $I^2 = 88\%$ for AMCI, and $I^2 = \text{NA}\%$ for MFX. Overall heterogeneity was $I^2 = 95\%$.

Visual Analog Scale

Postoperative VAS scores were reported in 11 studies, with mean values ranging from 0.6 to 36.2 points.[7,18,20,27,31,33,37,39,48,49,52] By subgroup, mean scores ranged from 2.0 to 18.3 points for ACI, 0.8 to 6.1 points for MACI, 0.6 to 4.1 points for AMCI, and 4.5 to 36.2 points for MFX. Heterogeneity was $I^2 = 99\%$ for ACI, $I^2 = 98\%$ for

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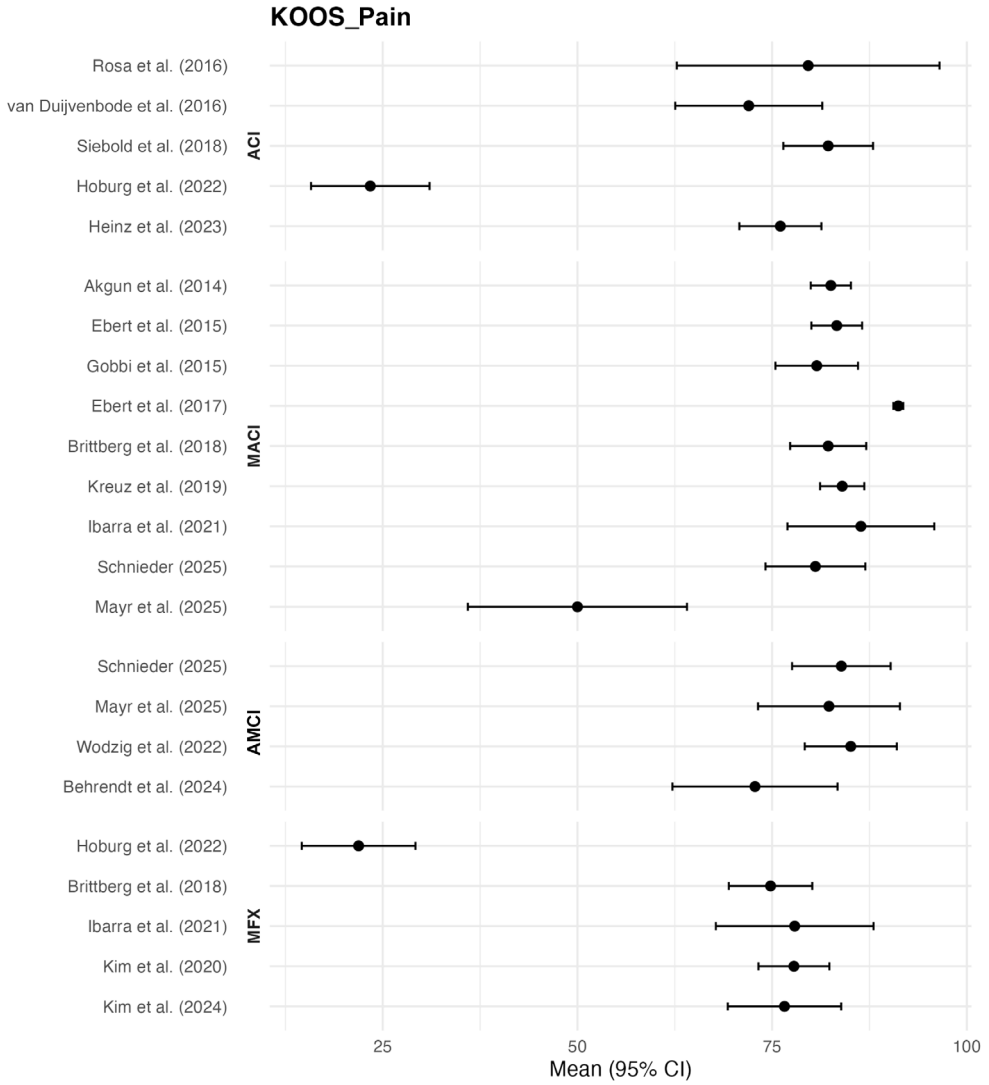

FIGURE 4 Forest plot illustrating postoperative KOOS Pain subscores with 95% CIs. Each horizontal line represents 1 study's mean postoperative KOOS Pain subscore with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were omitted given substantial heterogeneity (overall $I^2 = 99\%$). Overlapping CIs across treatment groups suggest comparable postoperative pain outcomes at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; AMCI, autologous minced cartilage implantation; CI, confidence interval; KOOS, Knee Injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture.)

MACI, $I^2 = 94\%$ for AMCI, and $I^2 = 91\%$ for MFX. Overall heterogeneity was $I^2 = 100\%$.

Minimal Clinically Important Difference, Patient Acceptable Symptom State, and Substantial Clinical Benefit

None of the included studies reported patient-level achievement of minimal clinically important difference, patient acceptable symptom state, or substantial clinical benefit thresholds for any PROM. Given the heterogeneity of preoperative PROM reporting across studies and the absence of individual patient data, these metrics could not be calculated at the study level. This represents a limitation of the existing literature and underscores the need for future studies to report these clinically meaningful benchmarks.

Adverse Events

Across all treatment groups, the overall failure rate was low (2.60%), with most failures occurring in ACI/MACI cohorts (3.21%) and few in MFX (1.32%) or AMCI (0%). A total of 179 reoperations were reported, most frequently for debridement or arthroscopy, followed by arthroplasty and marrow stimulation procedures.

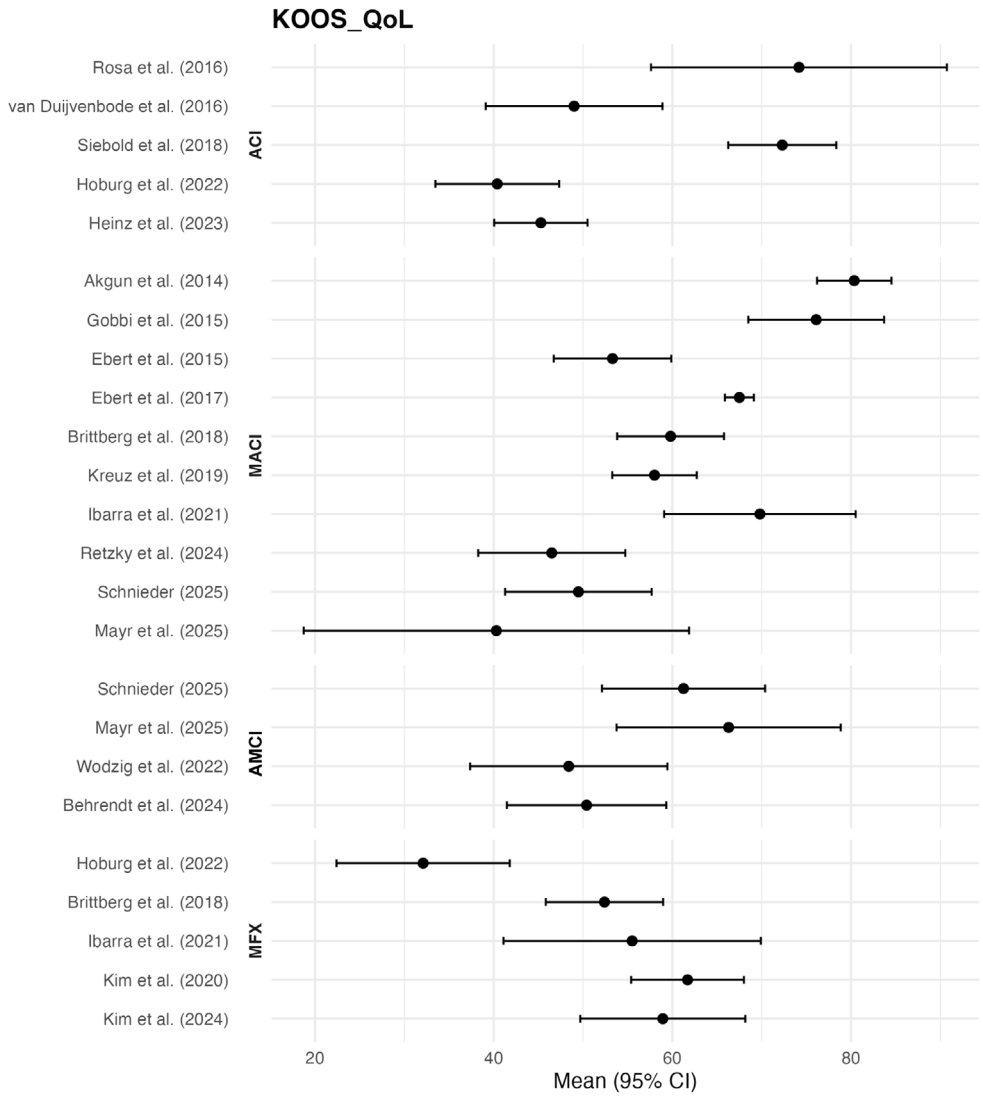

FIGURE 5 Forest plot illustrating postoperative KOOS QoL subscores with 95% CIs. Each horizontal line represents 1 study's mean postoperative KOOS QoL subscore with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were omitted given substantial heterogeneity (overall $I^2 = 93\%$). Overlapping CIs across groups suggest comparable postoperative QoL at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; AMCI, autologous minced cartilage implantation; CI, confidence interval; KOOS, Knee Injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture; QoL, Quality of Life.)

Adverse events were similarly most common in ACI/MACI (n = 429), with substantially fewer events in AMCI (n = 10) and MFX (n = 14). These trends reflect a generally favorable safety profile across all techniques, with AMCI showing the lowest rates of reoperation and complications.

DISCUSSION

The principal finding of this systematic review was that AMCI produced short- to midterm clinical outcomes comparable to those of ACI, MACI, and MFX. Across all included studies, PROMs such as IKDC, KOOS subscores, Lysholm, Tegner, and VAS pain showed substantial overlap across interventions. Qualitative analysis suggests that among AMCI, MFX, and traditional cell-based therapies, no single cartilage technique showed clear superiority in functional or pain outcomes at minimum 1-year follow-up.

When comparing ACI/MACI and MFX, no qualitative differences were observed in functional or pain outcomes within the present review. These findings align with prior comparative analyses showing similar short-term improvements between cell-based and marrow-stimulation approaches.[55,56] However, long-term data have suggested that MFX results often deteriorate over time

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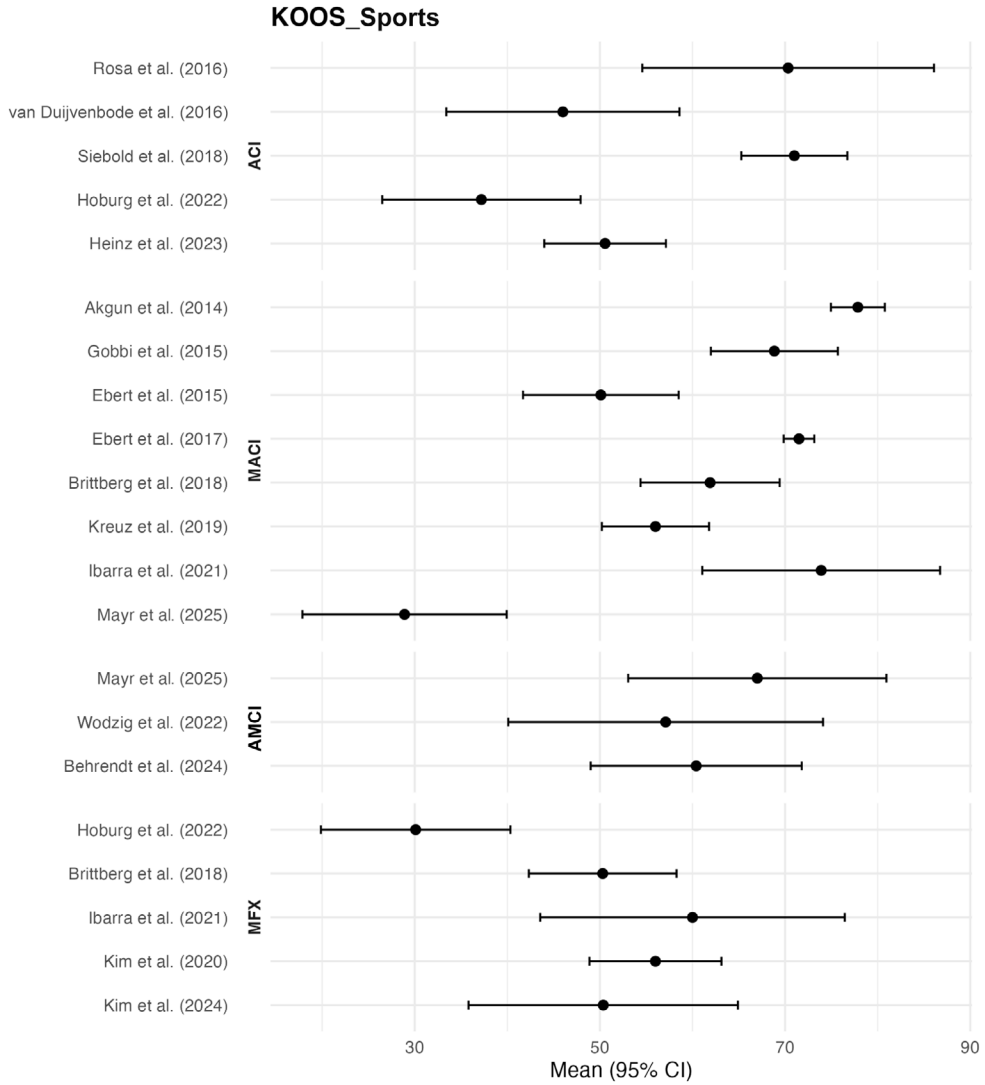

FIGURE 6 Forest plot illustrating postoperative KOOS Sports subscores with 95% CIs. Each horizontal line represents 1 study's mean postoperative KOOS Sports subscore with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were omitted given substantial heterogeneity (overall $I^2 = 94\%$). Overlapping CIs across groups suggest comparable postoperative sports-related function at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; AMCI, autologous minced cartilage implantation; CI, confidence interval; KOOS, Knee Injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture.)

because of fibrocartilage formation and subchondral bone changes.[1,57] Collectively, these data suggest that short-term recovery may be similar.

When comparing ACI/MACI and AMCI, short- to mid-term outcomes were also comparable across PROMs. Despite variability in harvest, fragmentation, and fixation techniques, mean improvements in KOOS, IKDC, and Lysholm scores were largely equivalent. These findings are consistent with previous literature that have shown comparable outcomes between AMCI and ACI/MACI.[3,58,59] Some studies have suggested that AMCI may lead to superior improvements compared with ACI; however, inconsistency in AMCI technique and insufficient long-term data limit the ability to draw definitive conclusions regarding its comparative efficacy and durability.[13] Nonetheless, ACI and MACI remain supported by more extensive long-term clinical and radiological data.[29,60,61] From a clinical standpoint, AMCI offers practical advantages as a single-stage, autologous technique that eliminates the need for cell culture and reduces cost, while achieving comparable early functional gains.[3,59,62] Notably, because preoperative PROM values were inconsistently reported across studies, this review focused on final follow-up scores rather than change scores. Although comparable final follow-up values suggest similar clinical endpoints, the magnitude of improvement from baseline could not be determined, and minimal clinically important difference could not be calculated for

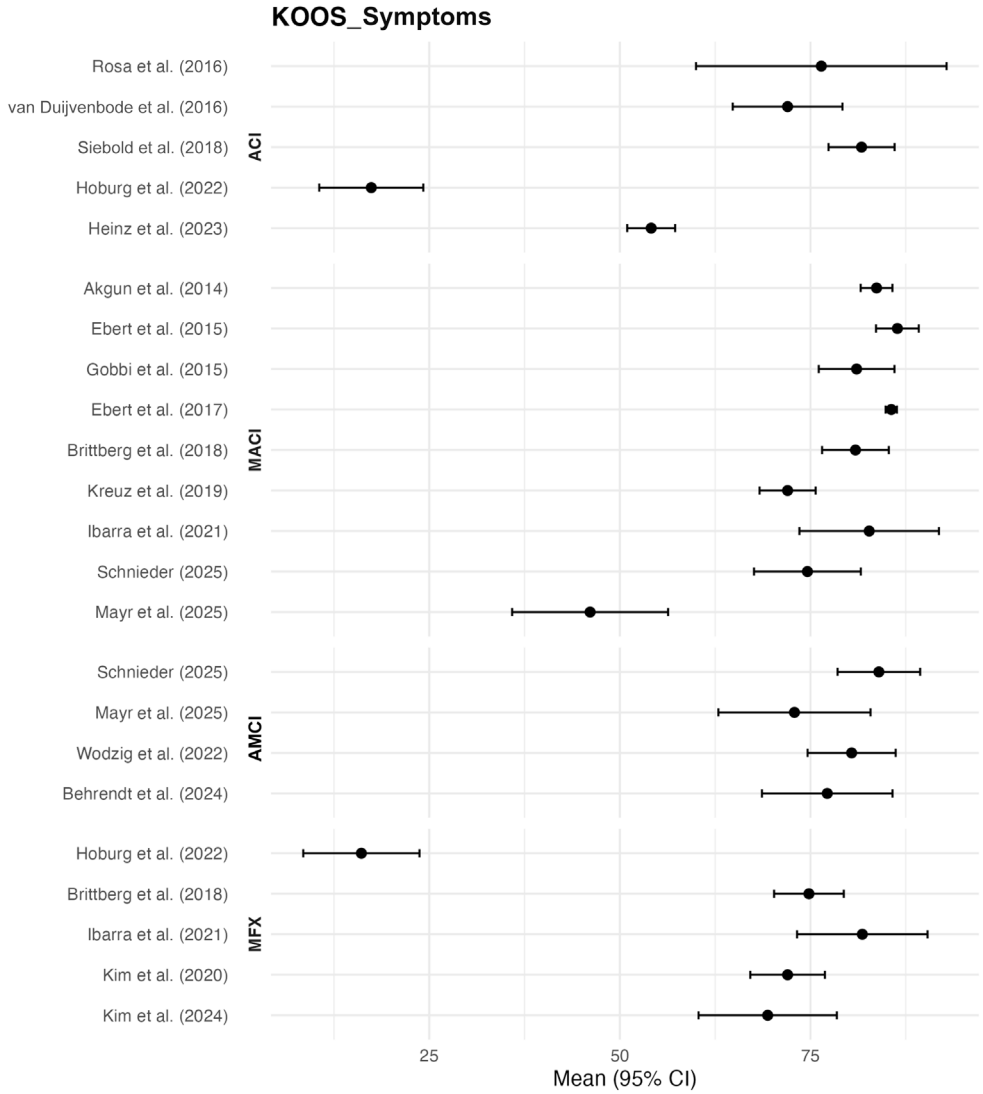

FIGURE 7 Forest plot illustrating postoperative KOOS Symptoms subscores with 95% CIs. Each horizontal line represents 1 study's mean postoperative KOOS Symptoms subscore with its 95% CI. Studies are grouped by treatment: ACI, MACI, AMCI, and MFX. Pooled weighted means were omitted given substantial heterogeneity (overall $I^2 = 99\%$). Overlapping CIs across groups suggest comparable postoperative symptom outcomes at short- to midterm follow-up. (ACI, autologous chondrocyte implantation; AMCI, autologous minced cartilage implantation; CI, confidence interval; KOOS, Knee Injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; MFX, microfracture.)

any group. It should also be noted that the AMCI cohort tended to have higher baseline IKDC and KOOS scores relative to ACI/MACI and MFX cohorts in studies that did report preoperative data, which may reflect differences in patient selection and could influence the observed magnitude of change. Future studies with standardized preoperative reporting are needed to enable more robust comparisons of treatment effect size. Further comparative studies, especially in long-term settings, are necessary to examine meaningful differences between these 2 techniques.

Comparisons between AMCI and MFX also showed no significant qualitative differences in PROMs at final follow-up. However, several previous studies have reported trends favoring AMCI at 2-year follow-up.[63,64] Prior reviews have noted that MFX often yields fibrocartilage repair tissue, which can deteriorate within 2 to 5 years, whereas minced cartilage techniques may promote more hyaline-like regeneration through viable chondrocyte migration and matrix integration.[59,65,66] However, comparative data remain limited, necessitating further examination of meaningful clinical differences between AMCI and MFX.

Limitations

This systematic review has several limitations. The included studies exhibited heterogeneity in design,

patient populations, lesion characteristics, and concomitant procedures, with evidence levels ranging from I to IV. Variation in outcome definitions, follow-up duration, and timing of assessments limited direct comparison across cohorts. Inconsistent reporting of failure criteria and the lack of standardized subgroup analyses further reduced comparability. Additionally, few studies provided direct head-to-head comparisons between techniques, and results were synthesized qualitatively rather than through formal meta-analysis because of methodological heterogeneity. These factors should be considered when interpreting the findings and their generalizability.

CONCLUSIONS

AMCI shows clinical outcomes that are at least comparable to ACI, MACI, and MFX and may be an appropriate alternative treatment for focal chondral defects of the knee. However, available studies are heterogeneous, and long-term data for AMCI remain limited.

DISCLOSURES

The author (B.J.C.) declares the following financial interests/personal relationships which may be considered as potential competing interests: B.J.C. reports a relationship with B Braun Aesculap Japan, Medipost, the *American Journal of Sports Medicine*, the *Journal of the American Academy of Orthopaedic Surgeons*, and the National Institutes of Health that includes nonfinancial support; Arthrex that includes consulting or advisory and nonfinancial support; Elsevier that includes funding grants and nonfinancial support; JRF Ortho that includes funding grants; OSSIO that includes equity or stocks. The other authors (B.E.C., K.S.S., J.E.J., D.S., Y.N.M., J.S., S.A., K.N.K.) declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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