Patellofemoral Cartilage Restoration

CME

A Systematic Review and Meta-analysis of Clinical Outcomes

Betina B. Hinckel,*† MD, PhD, Eli L. Pratte,‡ BS, Charles A. Baumann,‡ BS, Anirudh K. Gowd,§ MD, Jack Farr,‖ MD, Joseph N. Liu,¶ MD, Adam B. Yanke,# MD, PhD, Jorge Chahla,# MD, PhD, and Seth L. Sherman,** MD
Investigation performed at the University of Missouri, Columbia, Missouri, USA

Background: Many surgical options for treating patellofemoral (PF) cartilage lesions are available but with limited evidence comparing their results.

Purpose: To determine and compare outcomes of PF cartilage restoration techniques.

Study Design: Systematic review and meta-analysis.

Methods: PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) guidelines were followed by utilizing the PubMed, EMBASE, and Cochrane Library databases. Inclusion criteria were clinical studies in the English language, patient-reported outcomes after PF cartilage restoration surgery, and >12 months' follow-up. Quality assessment was performed with the Coleman Methodology Score. Techniques were grouped as osteochondral allograft transplantation (OCA), osteochondral autograft transfer (OAT), chondrocyte cell–based therapy, bone marrow–based therapy, and scaffolds.

Results: A total of 59 articles were included. The mean Coleman Methodology Score was 71.8. There were 1937 lesions (1077 patellar, 390 trochlear, and 172 bipolar; 298 unspecified). The frequency of the procedures was as follows, in descending order: chondrocyte cell–based therapy (65.7%), bone marrow–based therapy (17.2%), OAT (8%), OCA (6.6%), and scaffolds (2.2%). When compared with the overall pooled lesion size (3.9 cm^2; 95% CI, 3.5-4.3 cm^2), scaffold (2.2 cm^2; 95% CI, 1.8-2.5 cm^2) and OAT (1.5 cm^2; 95% CI, 1.1-1.9 cm^2) lesions were smaller ($P < .001$), while chondrocyte cell–based therapy lesions were larger (4.7 cm^2; 95% CI, 4.1-5.3 cm^2; $P = .039$). Overall, the instability pool was 11.9%, and the anatomic risk factors pool was 32.1%. Statistically significant improvement was observed on at least 1 patient-reported outcome in chondrocyte cell–based therapy (83%), OAT (78%), OCA (71%), bone marrow–based therapy (64%), and scaffolds (50%). There were no significant differences between any group and the overall pooled change in International Knee Documentation Committee score (30.2; 95% CI, 27.4-32.9) and Lysholm score (25.2; 95% CI, 16.9-33.5). There were no significant differences between any group and the overall pooled rate in minor complication rate (7.6%; 95% CI, 4.7%-11.9%) and major complication rate (8.3%; 95% CI, 5.7%-12.0%); however, OCA had a significantly greater failure rate (22.7%; 95% CI, 14.6%-33.4%) as compared with the overall rate (6.8%; 95% CI, 4.7%-9.5%).

Conclusion: PF cartilage restoration leads to improved clinical outcomes, with low rates of minor and major complications. There was no difference among techniques; however, failures were higher with OCA.

Keywords: knee; cartilage; patella; trochlea; patellofemoral; clinical outcomes; cartilage restoration; systematic review; meta-analysis

Focal chondral and osteochondral defects of the knee are common injuries and can significantly impair patients' quality of life.[1] Cartilage lesions are a common cause of knee morbidity in patients and are documented in 61% to 66% of reported knee arthroscopies, with a third of those being in the patellofemoral (PF) joint.[4,16,46] If cartilage lesions are not repaired, they can accelerate joint degeneration and lead to osteoarthritis.[57,60] Since articular cartilage is largely avascular and hypocellular, surgical intervention has become the primary method of restoration owing to the tissue's limited intrinsic healing.[36] The goal is to mitigate patients' pain and improve the physiological function of the affected joint, while possibly delaying and/or preventing the progression to arthritis and the need for knee arthroplasty.[50]

Many techniques have been described for cartilage restoration in the PF joint, including osteochondral allograft transplantation (OCA) and autologous chondrocyte implantation (ACI) among others.[34,42] Long-term improvement has been

The American Journal of Sports Medicine
2020;48(7):1756–1772
DOI: 10.1177/0363546519886853

described with these techniques.[7,12,38,63,67,73,83,85] In addition, recently other emerging techniques, such as bone marrow aspirate concentration (BMAC) implantation and particulated juvenile articular cartilage allograft (PJAC), have had increased utilization.[26,33,43-45,81,82] Consequently, there is extensive literature on the outcomes of cartilage repair surgery in the PF joint. However, there is a lack of studies that provide a summary and/or comparison of the results of these procedures.

The purpose of this systematic review and meta-analysis was to determine and compare outcomes of PF cartilage restoration techniques. We hypothesized that cartilage restoration of the PF joint would lead to favorable clinical outcomes with minimal complications.

METHODS

Literature Search

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines were followed during the database search.[64] An extensive literature search was conducted on October 8, 2018, in the PubMed, EMBASE, and Cochrane Library databases. We included studies that described outcomes for cartilage repair in the PF joint. Inclusion criteria were as follows: therapeutic studies with evidence levels 1, 2, 3, and 4 (randomized controlled trials, prospective cohort studies, case-control studies, and case series); treatment of full-thickness or nearly full-thickness cartilage lesions and osteochondral lesions; human participants; and English language. Exclusion criteria were as follows: <12 months of follow-up; <5 patients with PF lesions; the absence of any validated patient-reported outcomes (PROs); PROs that were not reported separately when PF was only a part of the cohort (unless authors directly provided those data); and studies that included identical participant populations, unless they evaluated different data parameters (when data were the same, we included the last follow-up). The search was conducted via a method grouping relevant terms by defect, location, and procedure. Relevant articles were determined to be those that included at least 1 term from each grouping:

Defect: cartilage lesion, chondral lesion, osteochondral lesion, cartilage defect, chondral defect, chondrocytes, osteochondritis dissecans, and osteochondral defect

Location: patella, trochlea, and patellofemoral

Procedure: cartilage repair, cartilage restoration, cartilage implantation, cartilage transplantation, implantation, transplantation, microfracture, autologous matrix-induced chondrogenesis, AMIC, autologous chondrocyte implantation, ACI, matrix-assisted autologous chondrocyte implantation, MACI, osteochondral autologous transfer, OATS, mosaicplasty, osteochondral allograft transplantation, Neocart, DeNovo, BioCartilage, Cartiform, and ProChondrix

Quality Assessment

The level of evidence of the articles was collected. The methodological quality of the articles included in this meta-analysis was assessed by the Coleman Methodology Score (CMS). Two authors independently applied the CMS (E.L.P. and C.A.B.), and a final score was reached by consensus. The CMS is computed by summation of 10 criteria (study size, follow-up, number of procedures, type of study, diagnostic certainty, description of surgical technique, rehabilitation and compliance, outcome criteria, outcome assessment, and selection process), leading to a total possible score of 100. The higher the score, the more probable the study avoids chance and other biases characteristic of poor methodology. Mean and standard deviation were calculated for each criterion. Also, publication bias was analyzed with a funnel plot.

Data Extraction and Analysis

All study data were extracted with a standardized predetermined criterion form: study (first author and year),

*Address correspondence to Betina B. Hinckel, MD, PhD, Department of Orthopaedic Surgery, William Beaumont Hospital, 10000 Telegraph Road, Suite 100, Taylor, MI 48180, USA (email: betinahinckel@me.com).
†Department of Orthopaedic Surgery, William Beaumont Hospital, Royal Oak, Michigan, USA.
‡School of Medicine, University of Missouri, Columbia, Missouri, USA.
§Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina, USA.
||OrthoIndy Knee Preservation and Cartilage Restoration, School of Medicine, Indiana University, Indianapolis, Indiana, USA.
¶Department of Orthopedic Surgery, Loma Linda University Medical Center, Loma Linda, California, USA.
#Rush University Medical Center, Chicago, Illinois, USA.
**Division of Sports, Department of Orthopedic Surgery, School of Medicine, Stanford University, Palo Alto, California, USA.
Submitted April 10, 2019; accepted August 27, 2019.
One or more of the authors has declared the following potential conflict of interest or source of funding: S.L.S. has received consulting fees from Arthrex, Ceterix Orthopaedics, CONMED Linvatec, Flexion Therapeutics, GLG Consulting, JRF Ortho, Moximed, Olympus, and Vericel and has received research support from Arthrex. A.B.Y. has received consulting fees from JRF Ortho, Olympus, and Sparta Biomedical; research funding from Arthrex and Organogenesis; and is an investor in PatientIQ. J.F. has received research or institutional support from Active Implants, Arthrex, Ceterix, Fidia Pharma, Histogenics, Moximed Inc, Novartis Inc, Organogenesis Inc, TRX, Orthopaedics Inc, and ZimmerBiomet; has received miscellaneous nonincome support, commercially derived honoraria, or other nonresearch-related funding from Arthrex, MedShape Inc, Regentis, Samumed Inc, Vericel, and ZimmerBiomet; has received royalties from Arthrex, DePuy Synthese Products Inc, Biopoly LLC, and Organogenesis; holds stock or stock options in MedShape Inc and OrthoRegenerative Technologies Inc; and is a consultant for or on the advisory board of Aesculap, Arthrex Inc, Cartiheal, Exactech, JRF Ortho, Moximed Inc, Organogenesis Inc, Samumed Inc, TRX Orthopedics Inc, Vericel, ZimmerBiomet, Zipline Medical, and ZKR Orthopedics Inc. B.B.H. has received education, hospitality, and travel payments from Arthrex and education payments from Elite Orthopaedics LLC. J.N.L. has received education, hospitality, and travel payments from Arthrex and Smith & Nephew and hospitality payments from Exactech and Wright Medical. J.C. has received education and hospitality payments from Arthrex and Smith & Nephew. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

technique used for the repair of the cartilage lesion, number of knees with PF lesions (sorted by sex if possible), location of PF lesions (patellar, trochlear, or bipolar), lesion size, follow-up, associated pathology, associated procedures, clinical results, complications, and failures. When standard deviation was not available, authors were contacted to request the remaining data.

To interpret and synthesize results, the techniques were grouped on the basis of their fundamental mechanism of action. The 5 groups were as follows:

- OCA transplantation
- Osteochondral autograft transfer (OAT)—as either a single cylinder transfer or a mosaicplasty
- Chondrocyte cell–based therapy—ACI with periosteum, ACI with membrane without chondrocytes already in the membrane, matrix-induced ACI (MACI), and PJAC
- Bone marrow–based therapy with or without orthobiologic augmentation—autologous matrix-induced chondrogenesis with or without platelet-rich plasma, BMAC implantation, microfracture
- Scaffolds—TruFit and 3-dimensional osteochondral scaffold

Under the subheading "associated PF pathology," *instability* was included when objective patellar subluxation or dislocation was reported (with or without PF risk factors) and *anatomic risk factors* when maltracking, malalignment, or PF risk factors without instability were reported. PF risk factors included increased lateral quadriceps vector, patella alta, increased lateral tilt, and trochlear dysplasia. Under the subheading "associated procedures," *realignment* procedures included tibial tuberosity osteotomies (TTOs), distal femoral osteotomy, Roux-Goldthwait, and other soft tissue extensor mechanism realignment; *trochleoplasty* included all trochleoplasty techniques; *soft tissue* procedures included medial PF ligament reconstructions and retinaculum releases; and *non-PF* procedures included other concomitantly performed procedures that did not affect the PF compartment.

Minor complications were considered the ones that did not require further surgical intervention, while major complications were the ones that did require surgical interventions (other than revisions of the cartilage restoration procedures). Interventions were considered failures when the additional surgical procedures were revisions of the cartilage restoration procedures, either with another cartilage restoration procedure or with PF arthroplasty or total knee arthroplasty.

The term *study* is used distinctly from *article* in our analysis. *Study* refers to each technique or lesion location within an article that reports a PRO. Therefore, some articles included only 1 study; however, some articles had numerous studies (ie, if they reported separate PROs for numerous lesion locations within the PF joint or compared techniques). When >1 technique was utilized in 1 study, the data from each technique were reported in the appropriate group. In a similar manner, when data from >1 location within the PF joint (patellar, trochlear, or bipolar) were reported, the data from each lesion location were reported separately in the appropriate group.

Statistical Analysis

The metafor package as part of RStudio software (v 1.0.143; R Foundation for Statistical Computing) was used for data analysis. Each article was stratified by procedure. Forest plots were created for lesion size, major and minor complications, failures, and change in International Knee Documentation Committee (IKDC), Cincinnati, and Lysholm scores. Predicted meta-regressions for each group were compared against the meta-regression for the overall population to demonstrate any deviation by using a Wald test.[80] Pairwise comparison of each group was performed with the Wald test to determine differences in associated PF pathology and associated procedures. The I^2 index was used to measure heterogeneity of included studies.[41] Effect sizes were calculated with random effects models via the DerSimonian-Laird estimator.[18,77] A random effects model was used to plot data with high heterogeneity, while a fixed effects model was used for data with low heterogeneity.[9] Articles with comparative groups were separated into homogeneous techniques. All outcomes of analysis were reported as the weighted mean with a 95% CI. A funnel chart was used to evaluate publication bias. The estimated treatment effect was plotted on the *x*-axis, while the size of each study was plotted on the *y*-axis. Smaller studies were plotted near the bottom, while larger studies were plotted at the top. Point estimates were checked to be distributed evenly and symmetrical around the real effect of treatment to determine if no bias existed.[78]

RESULTS

Literature Search

The initial review of the literature, with the predetermined search terms, yielded 1247 journal articles. Inclusion and exclusion criteria were met by 59 articles and 62 studies. The articles included in this study were published between 1999 and 2018. No randomized controlled trial was found in our search, and all articles were case series. The flowchart of search, exclusion, and inclusion is included in Figure 1.

Literature Quality Assessment

The level of evidence breakdown is as follows: level 1 (n = 0), level 2 (n = 12), level 3 (n = 3), and level 4 (n = 44). The mean CMS score was 71.8. From analysis of variance, there was no statistical difference in composite CMS score among subgroups (P = .260). A funnel plot demonstrates the publication bias (Figure 2). The pooled loss of reduction was calculated for each article used in the meta-analysis. Publication bias was best assessed from a funnel plot constructed from the pooled loss of reduction of all articles. Studies of larger effect sizes were plotted higher in the funnel, while those of lower effect sizes were plotted near the base. Studies were inherently heterogeneous from the different operative techniques performed for similar pathology.

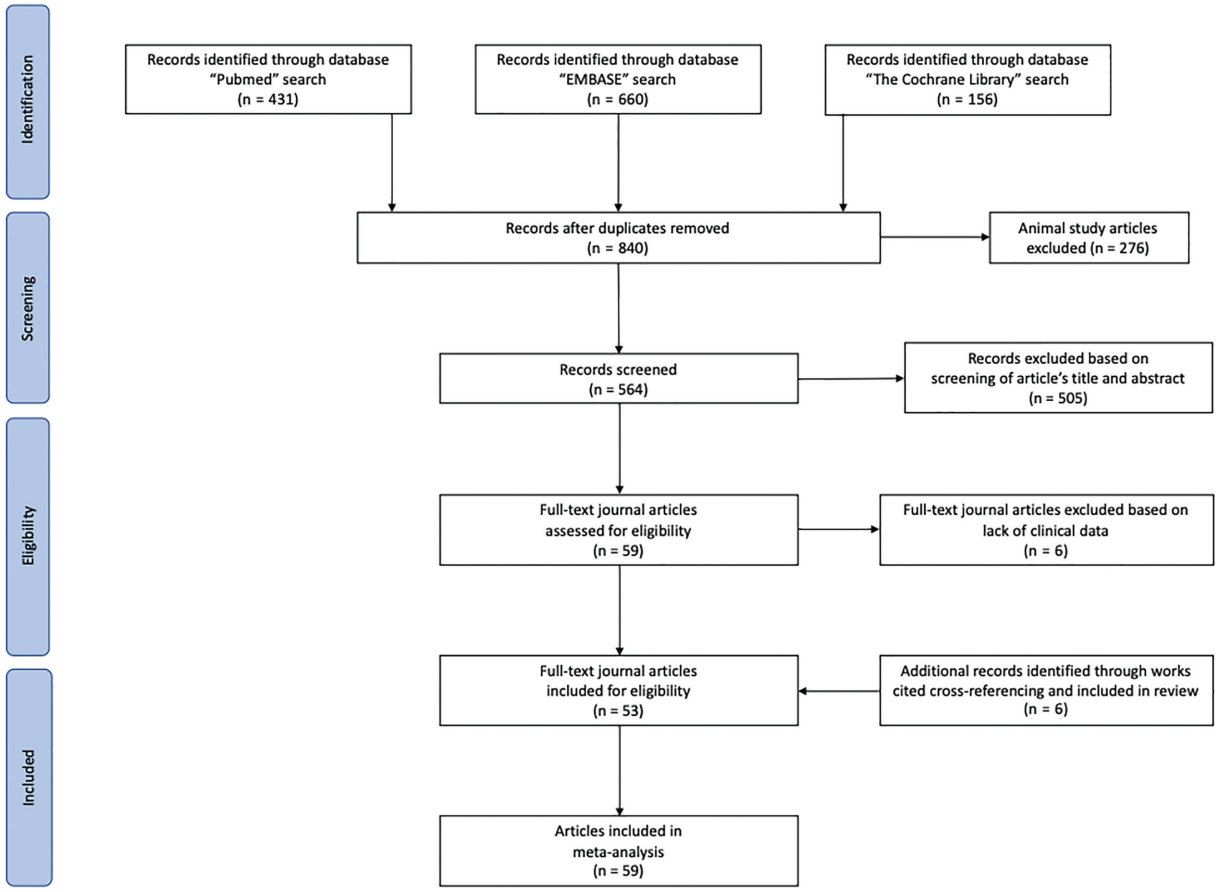

Figure 1. PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) flow diagram outlining meta-analysis algorithm.

Systematic Review Results

The frequency of procedures performed were as follows, in decreasing order (n = number of knees): chondrocyte cell–based therapy (n = 1274, 65.7%), bone marrow–based therapy with or without orthobiologic augmentation (n = 334, 17.2%), osteochondral autografts transfer (n = 156, 8%), OCA transplantation (n = 129, 6.6%), and scaffolds (n = 44, 2.2%) (Tables 1-5).

Lesion locations were as follows (n = number of knees): patellar lesions (n = 1077, 65.7%), trochlear lesions (n = 390, 23.8%), and bipolar lesions (n = 172, 10.5%). Bipolar lesions were not included in the patellar or trochlear lesion numbers. Specific lesion location within the PF joint was not reported in 298 lesions. All but the scaffolds group included patellar, trochlear, and bipolar lesions.

Instability was reported in 167 knees (18.5% of the 905 that acknowledged instability), and anatomic risk factors were reported in 698 knees (43.5% of the 1603 that acknowledged anatomic risk factors). Although reporting of risk factors by the included articles was variable, examples of the more common anatomic risk factors were tibial tuberosity–trochlear groove >15 to 20 mm, tilt >10° to 20°, valgus >5°, and trochlea dysplasia.

The most common PROs were IKDC (26 studies), Lysholm (21 studies), and Modified Cincinnati (15 studies). Statistically

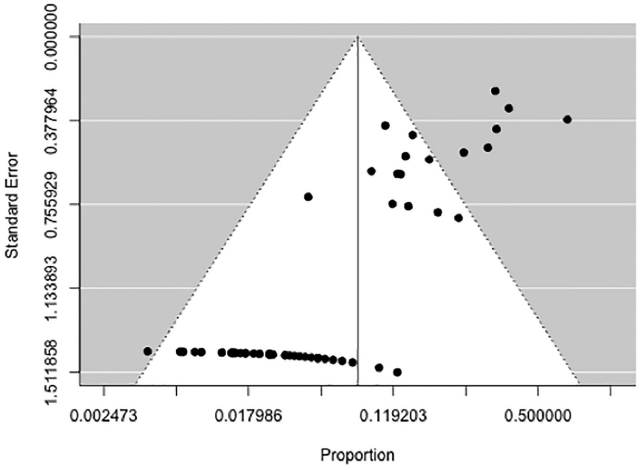

Figure 2. Funnel plot of publication bias for all articles included in meta-analysis.

significant improvement was observed on at least 1 PRO in chondrocyte cell–based therapy (30 studies, 83%), OAT (7 studies, 78%), OCA (5 studies, 71%), bone marrow–based therapy (7 studies, 64%), and scaffolds (1 study, 50%).

TABLE 1
Results of Patellofemoral Cartilage Restoration: OCA (n = 129, 6.6%)[a]

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Jamali (2005)[47]	OCA	20	P, BP	Nm	94	Instability: Nm, anatomic risk factors: 20	Realignment: 0, trochleoplasty: 0, soft tissue: 9, non-PF: 0	Mod Merle d'Aubigné-Postel: 3.85	Minor: 0, major: 0, failures: 5 (25)	Case series, CMS: 59, LOE: 4
Torga Spak (2006)[83]	OCA	14	P, BP	Nm	110	Instability: 14, anatomic risk factors: 14	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Lysholm: 52.5	Minor: 0, major: 0, failures: 2 (14.3)	Case series, CMS: 56, LOE: 4
Gracitelli (2015)[39]	OCA	28	P	10.1	116.4	Instability: 1, anatomic risk factors: 3	Realignment: 4, trochleoplasty: 0, soft tissue: 8, non-PF: 1	IKDC: 30[b]	Minor: 0, major: 0, failures: 8 (28.6)	Case series, CMS: 65, LOE: 4
Cameron (2016)[12]	OCA	29	T	6.1	84	Instability: Nm, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 1, soft tissue: 7, non-PF: 2	IKDC function: 40,[b] IKDC pain: –27[b]	Minor: 0 (3.4), major: 5 (17.2), failures: 1 (3.4)	Case series, CMS: 65, LOE: 4
Frank (2017)[30]	OCA	8	P, T	10.1	59.8	Instability: Nm, anatomic risk factors: Nm	Realignment: 4, trochleoplasty: 0, soft tissue: 0, non-PF: 1	IKDC: 36.95,[b] Lysholm: 31.79[b]	Minor: 1 (12.5), major: 2 (25), failures: 2 (25)	Prospective, case series, CMS: 74, LOE: 2
Wang (2018)[89]	OCA	10	T	7.4	49.2	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 25.8[b]	Minor: 0, major: 2 (20), failures: 1 (10)	Prospective, case series, CMS: 76, LOE: 2
Wang (2018)[88]	OCA	23	P, T, BP	7.1	43.2	Instability: Nm, anatomic risk factors: 2	Realignment: 1, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 16.1[b]	Minor: 0, major: 3 (13), failures: 8 (34.8)	Prospective, case series, CMS: 80, LOE: 2
7 studies	OCA	129	P, T, BP	6.1-10.1	43.2-116.4	Instability: 15, anatomic risk factors: 39	Realignment: 9, trochleoplasty: 1, soft tissue: 24, non-PF: 4	Outcomes improvement: 5 (71%), no difference: 2 (29%)	Minor: 1 (0.7), major: 12 (9.3), failures: 27 (20.9)	CMS: 67.9 (56-80), LOE: 2 (n = 3) and 4 (n = 4)

[a]BP, bipolar lesion; CMS, Coleman Methodology Score; IKDC, International Knee Documentation Committee; LOE, level of evidence; Nm, not mentioned; OCA, osteochondral allograft transplantation; P, patellar lesion; PF, patellofemoral (location not specified); PRO, patient-reported outcome; T, trochlear lesion.
[b]Statistically significant finding.

Overall, there were 127 (8.6%) major complications. For comparison among major complications, the following groups were created: problems with range of motion (n = 38, 32.2%), which includes manipulation under anesthesia as well as arthroscopy for arthrofibrosis or scar tissue removal related to limited range of motion; arthroscopy for debridement (n = 34, 28.8%), which includes chondroplasty and any other graft-related debridement; and hardware removal (n = 35, 29.7%). The minor complications (n = 163, 11.1%) were more variable than the major complications, but the most important complications reported were graft hypertrophy, deep vein thrombosis, quadriceps weakness, and superficial infection.

Relevant and summarized data of the studies are reported in Tables 1 to 5. Techniques are grouped as previously described.

Variables Analysis

Age. In studies with mean ages from 29.9 to 45.5 years, age was found not to influence clinical outcomes in ACI,[25,35,73] PJAC,[90] and MACI and BMAC implantation.[33] Wang et al[90] additionally found no differences in magnetic resonance imaging (MRI) scores when comparing patients aged <30 years and ≥30 years. However, Niemeyer et al[68] found that age affected outcomes in patients with ACI in the patella.

Sex. Farr[25] and Gomoll et al[35] found sex not to influence results in patients treated with ACI, while Perdisa et al[70] found women to have worse outcomes in patients treated with a scaffold.

Etiology. Tompkins et al[82] found that patients treated with PJAC who had patellar instability had higher activity levels per the Tegner score than the ones with chronic PF pain, but there were no differences in other scores. Gobbi et al[33] found etiology not to influence outcomes in patients treated with MACI or BMAC implantation.

Tibiofemoral vs Patellofemoral. Cvetanovich et al,[17] comparing ACI in femoral condyles and ACI in the PF (65% of associated TTO), found that both groups improved, with no differences in the amount of improvement.

Bipolar vs Unipolar. In patients treated with ACI, Peterson et al[73] found bipolar lesions to have worse outcomes than unipolar, while Gomoll et al[35] found no differences.

Trochlea vs Patella. Filardo et al[28] found that MACI in the trochlea had better PROs and sports activities than in the patella. In a multivariate analysis considering lesion site, sex, and realignment procedures, it was confirmed that lesion site was the most important variable to determine the outcome. In addition, Gobbi et al[33] found that

TABLE 2
Results of Patellofemoral Cartilage Restoration: OAT (n = 156, 8%)[a]

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Nho (2008)[66]	OAT-M	22	P	1.656	28.7	Instability: 2, anatomic risk factors: 9	Realignment: 12, trochleoplasty: 0, soft tissue: 13, non-PF: 0	IKDC: 27.2[b]	Minor: 0, major: 4 (18.2), failures: 0	Case series, CMS: 80, LOE: 4
Visonà (2010)[86]	OAT-M	6	P	0.84	26	Instability: 1, anatomic risk factors: 2	Realignment: 1, trochleoplasty: 0, soft tissue: 3, non-PF: 0	IKDC: 29.1, Lysholm: 26.7	Minor: 0, major: 0, failures: 0	Case series, CMS: 61, LOE: 4
Figueroa (2011)[27]	OAT-1	10	P	1.2	37.3	Instability: 10, anatomic risk factors: 6	Realignment: 1, trochleoplasty: 0, soft tissue: 6, non-PF: 0	IKDC postoperative: 93.6,[c] Lysholm: 16.7	Minor: 8 (80), major: 0, failures: 0	Prospective case series, CMS: 66, LOE: 2
Cohen (2012)[15]	OAT-1	17	P	1.5	19.8	Instability: Nm, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 0, soft tissue: 7, non-PF: 0	Lysholm: 21.17[b]	Minor: Nm, major: Nm, failures: Nm	Prospective cohort, CMS: 73, LOE: 2
Astur (2014)[5]	OAT-1	33	P	1.5	30.2	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Lysholm: 23.49[b]	Minor: 0, major: 3 (9.1), failures: 0	Case series, CMS: 80, LOE: 4
Emre (2017)[23]	OAT-M	33	P, T	2.4	19.3	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Lysholm: 36.3[b]	Minor: 5 (15.2), major: 0, failures: 0	Case series, CMS: 55, LOE: 4
Astur (2017)[6]	OAT-1	20	P	1.16	24	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Kujala: 21[b]	Minor: 14 (70), major: 0, failures: 0	Case series, CMS: 80, LOE: 4
Chadli (2017)[13]	OAT-M	8	P	Nm	28.6	Instability: 1, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 36.2,[b] Lysholm: 34.5[b]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 51, LOE: 4
Yabumoto (2017)[92]	OAT-1, OAT-M[d]	7	BP	4.31	46.9	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Normal or nearly normal IKDC: 57.1%[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 61, LOE: 4
9 studies	OAT-1, OAT-M	156	P, T, BP	0.84-4.31	19.3-46.9	Instability: 14, anatomic risk factors: 17	Realignment: 14, trochleoplasty: 0, soft tissue: 29, non-PF: 0	Outcomes improvement: 7 (78%), no difference: 2 (22%)	Minor: 27 (20.6), major: 7 (5.3), failures: 0 (0)	CMS: 67.4 (51-80), LOE: 2 (n = 2) and 4 (n = 7)

[a]BP, bipolar lesion; CMS, Coleman Methodology Score; IKDC, International Knee Documentation Committee; LOE, level of evidence; Nm, not mentioned; OAT-1, osteochondral autograft transfer (1 cylinder); OAT-M, osteochondral autograft transfer (mosaicplasty); P, patellar lesion; PF, patellofemoral (location not specified); PRO, patient-reported outcome; T, trochlear lesion.
[b]Statistically significant finding.
[c]Preoperative values were not given; therefore, the Δ in PROs could not be calculated, and the included values are postoperative.
[d]A mixture of single and multiple plugs were used on the patient population. Results were not stratified by the number of osteochondral plugs.

outcomes with MACI in the patella deteriorated after 2 years as compared with trochlea. However, Wang et al[90] found no differences in PJAC clinical and MRI outcomes between the trochlea and patella, as did Farr[25] for ACI.

Location in the Patella. In patients treated with ACI and concomitant TTO as indicated, Gillogly and Arnold,[32] Gomoll et al,[35] Farr,[25] and Vanlauwe et al[84] found no differences in regard to location. However, Niemeyer et al[68] found that ACI in patients with patellar lesions, without maltracking and no concomitant TTO, had better outcomes for defects located on the lateral facet than for those on the medial facet or involving both facets. As well, Astur et al[5] found better results after OAT in the lateral facet as compared with combined medial and lateral lesions.

Lesion Size. Farr[25] and Gomoll et al[35] found lesion size not to influence results in patients treated with ACI. However, Niemeyer et al[68] found that ACI in patients with patellar defect, without maltracking and no concomitant TTO, had worse results in larger lesions, and Gobbi et al[33] found patients with MACI had worsened VAS scores after 2 years in lesions >10 cm^2 versus ≤ 10 cm^2.

Tibial Tuberosity Osteotomy. When TTO was performed selectively to correct maltracking, various authors found no differences in clinical outcomes between those patients who had TTO and those who did not, as associated with ACI,[25,35,69,73,84] scaffolds,[70] and PJAC.[90] Wang et al[90] additionally found no differences in MRI scores. Tompkins et al[82] found that patients treated with PJAC and concomitant TTO had lower VAS scores, but there were no differences in other scores.

Combined Factors. Kon et al[51] found that MACI in women with patellar lesions requiring realignment had a combination of factors that synergistically led to worse outcomes among PF cartilage lesions. Kreuz et al[53] also

TABLE 3
Results of Patellofemoral Cartilage Restoration: Chondrocyte Cell–Based Therapy (n = 1274, 65.7%)[a]

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Alfredson and Lorentzon (1999)[2]	pACI	57	P	7.63	40.68	Instability: 10, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Nm	Minor: 3 (5.3), major: 0, failures: 0	Case series, CMS: 68, LOE: 4
Peterson (2000)[72]	pACI	34	P, BP	4.66	32.4	Instability: Nm, anatomic risk factors: 19	Realignment: 19, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Nm	Minor: 4 (11.8), major: 0, failures: 2 (5.9)	Case series, CMS: 59, LOE: 4
Peterson (2002)[71]	pACI	17	P	Nm	88.8	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 50[b]	Minor: 0, major: 2 (11.8), failures: 0	Case series, CMS: 61, LOE: 4
Minas (2005)[62]	pACI	8	P	4.34	46.4	Instability: 0, anatomic risk factors: 5	Realignment: 5, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 15[b]	Minor: 0, major: 0, failures: 4 (50)	Prospective cohort, CMS: 80, LOE: 2
Minas (2005)[62]	pACI	9	T	4.74	46.4	Instability: 0, anatomic risk factors: 6	Realignment: 6, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 16.6[b]	Minor: 0, major: 0, failures: 2 (22.2)	Prospective cohort, CMS: 80, LOE: 2
Minas (2005)[62]	pACI	4	BP	12.59	46.4	Instability: 0, anatomic risk factors: 3	Realignment: 3, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 17.5[b]	Minor: 0, major: 0, failures: 2 (50)	Prospective cohort, CMS: 80, LOE: 2
Henderson and Lavigne (2006)[40]	pACI	50	P, BP	3.07	27.55	Instability: Nm, anatomic risk factors: 22	Realignment: 22, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 25.8,[b] Mod Cincinnati: 31[b]	Minor: 26 (52), major: 2 (4), failures: 0	Retrospective comparative study, CMS: 83, LOE: 3
Kreuz (2007)[54]	pACI	27	P, T	6.42	36	Instability: Nm, anatomic risk factors: 0	Realignment: Nm, trochleoplasty: Nm, soft tissue: Nm, non-PF: Nm	Mod Cincinnati:, 14.8[b]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 78, LOE: 4
Mandelbaum (2007)[59]	pACI	40	T	4.5	59	Instability: Nm, anatomic risk factors: 8	Realignment: 11, trochleoplasty: 0, soft tissue: 0, non-PF: 14	Mod Cincinnati: 33[b]	Minor: 16 (40), major: 6 (15), failures: 0	Case series, CMS: 60, LOE: 4
Farr (2007)[25]	pACI	39	P, T, BP	5.5	37.2	Instability: 28, anatomic risk factors: Nm	Realignment: 28, trochleoplasty: 0, soft tissue: 6, non-PF: 1	Lysholm: 30,[b] Mod Cincinnati: 20[b]	Minor: 29 (74.4), major: 0, failures: 0	Case series, CMS: 80, LOE: 4
Steinwachs and Kreuz (2007)[79]	mACI	19	P	6.07	36	Instability: Nm, anatomic risk factors: Nm	Realignment: Nm, trochleoplasty: Nm, soft tissue: Nm, non-PF: Nm	Mod Cincinnati: 20	Minor: 0, major: 0, failures: 0	Case series, CMS: 80, LOE: 4
Steinwachs and Kreuz (2007)[79]	mACI	10	T	6.26	36	Instability: Nm, anatomic risk factors: Nm	Realignment: Nm, trochleoplasty: Nm, soft tissue: Nm, non-PF: Nm	Mod Cincinnati: 51[b]	Minor: 0, major: 0, failures: 1 (10)	Case series, CMS: 80, LOE: 4
Niemeyer (2008)[68]	pACI, mACI, MACI[c]	70	P	4.41	38.4	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC postoperative: 62,[d] Lysholm postoperative: 73,[d] Mod Cincinnati: 27.06[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 71, LOE: 4
Pascual-Garrido (2009)[69]	pACI	52	P, T, BP	4.2	48	Instability: 1, anatomic risk factors: Nm	Realignment: 28, trochleoplasty: 0, soft tissue: 4, non-PF: 3	IKDC: 26,[b] Lysholm: 26,[b] Mod Cincinnati: 20[b]	Minor: 0, major: 0, failures: 4 (7.7)	Case series, CMS: 83, LOE: 4
Gigante (2009)[31]	MACI	14	P, BP	Nm	36	Instability: 3, anatomic risk factors: 14	Realignment: 14, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Lysholm: 37.5,[b] Mod Cincinnati: 60[b]	Minor: 1 (7.1), major: 2 (14.3), failures: 0	Prospective cohort, CMS: 76, LOE: 2
Peterson (2010)[73]	pACI	57	P, BP	7.18	153.6	Instability: Nm, anatomic risk factors: 25	Realignment: 30, trochleoplasty: 23, soft tissue: 2, non-PF:0	Lysholm: 3, Mod Cincinnati postoperative: 51[d]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 61, LOE: 4
Vasiliadis (2011)[85]	pACI	65	P, T, BP	5.5	151.2	Instability: Nm, anatomic risk factors: 65	Realignment: 27, trochleoplasty: 23, soft tissue: 73, non-PF: 0	Lysholm: 9.5	Minor: 29 (44.6), major: 7 (10.8), failures: 5 (7.7)	Case series, CMS: 51, LOE: 4
Macmull (2012)[58]	mACI	25	P	4.73	45	Instability: Nm, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 6.64	Minor: 0, major: 0, failures: 0	Case series, CMS: 83, LOE: 4

(continued)

TABLE 3
(continued)

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Macmull (2012)[58]	MACI	23	P	4.76	35.3	Instability: Nm, anatomic risk factors: Nm	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati: 13	Minor: 0, major: 0, failures: 0	Case series, CMS: 83, LOE: 4
Vanlauwe (2012)[84]	mACI	40	P, T, BP	4.89	37	Instability: Nm, anatomic risk factors: 12	Realignment: 12, trochleoplasty: 0, soft tissue: 0, non-PF: 0	KOOS: 25.7[b]	Minor: 9 (22.5), major: 16 (40), failures: 0	Case series, CMS: 80, LOE: 4
Teo (2013)[81]	pACI	20	P	Nm	72	Instability: 0, anatomic risk factors: 6	Realignment: 6, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 30,[b] Lysholm: 20[b]	Minor: 2 (10), major: 0, failures: 0	Case series, CMS: 65, LOE: 4
Kreuz (2013)[53]	MACI	20	P, T	5.4	48	Instability: Nm, anatomic risk factors: 0	Realignment: Nm, trochleoplasty: Nm, soft tissue: Nm, non-PF: Nm	IKDC: 22.12,[b] Lysholm: 26.8[b]	Minor: Nm, major: Nm, failures: Nm	Prospective cohort, CMS: 80, LOE: 2
Petri (2013)[74]	MACI	10	PF	3.4	36	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 29.6,[b] Lysholm: 21.1,[b] Mod Cincinnati: 24.7[b]	Minor: 0, major: 0, failures: 0	Retrospective match-pair analysis, CMS: 65, LOE: 4
Tompkins (2013)[82]	PJAC	15	P	2.4	28.8	Instability: 5, anatomic risk factors: Nm	Realignment: 3, trochleoplasty: 0, soft tissue: 5, non-PF: 0	IKDC postoperative: 73.3[d]	Minor: 5 (33.3), major: 0, failures: 0	Case series, CMS: 61, LOE: 4
Filardo (2014)[29]	MACI	49	P, T, BP	3	60	Instability: Nm, anatomic risk factors: 0	Realignment: 7, trochleoplasty: 1, soft tissue: 14, non-PF: 9	IKDC: 38.6[b]	Minor: Nm, major: Nm, failures: Nm	Cohort study, CMS: 83, LOE: 2
Gillogly and Arnold (2014)[32]	pACI	25	P	6.4	90.7	Instability: Nm, anatomic risk factors: 25	Realignment: 25, trochleoplasty: 4, soft tissue: 0, non-PF: 0	IKDC: 33,[b] Lysholm: 39,[b] Mod Cincinnati: 40[b]	Minor: 1 (4), major: 9 (36), failures: 1 (4)	Case series, CMS: 80, LOE: 4
Meyerkort (2014)[61]	MACI	24	P, T	3.5	60	Instability: Nm, anatomic risk factors: 9	Realignment: 7, trochleoplasty: 0, soft tissue: 7, non-PF: 0	KOOS ADL: 19,[b] KOOS Pain: 20.6,[b] KOOS QoL: 31.3,[b] SF-36 Physical: 8.7[b]	Minor: 6 (25), major: 3 (12.5), failures: 0	Case series, CMS: 80, LOE: 4
Gomoll (2014)[35]	pACI	110	P, BP	6.63	90	Instability: 75, anatomic risk factors: 75	Realignment: 75, trochleoplasty: 5, soft tissue: 46, non-PF: 22	IKDC: 29.2,[b] Mod Cincinnati: 30[b]	Minor: 0, major: 0, failures: 9 (8.2)	Case series, CMS: 86, LOE: 4
Gobbi (2015)[33]	MACI	19	P, T, BP	7.12	59.69	Instability: Nm, anatomic risk factors: 8	Realignment: 11, trochleoplasty: 0, soft tissue: 0, non-PF: 1	IKDC: 29.33[b]	Minor: 0, major: 4 (21.1), failures: 0	Prospective comparative study, CMS: 70, LOE: 3
Ebert (2015)[21]	MACI	47	P, T	3.3	>24	Instability: 0, anatomic risk factors: 19	Realignment: 19, trochleoplasty: 0, soft tissue: 0, non-PF: 0	KOOS ADL: 18.5,[b] KOOS Pain: 21.9,[b] KOOS QoL: 30.4,[b] SF-36 Physical: 12.2[b]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 83, LOE: 4
Müller (2015)[65]	MACI	16	P, T	5.6	48	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 27[b]	Minor: 0, major: 0, failures: 0	Prospective cohort, CMS: 76, LOE: 2
Kon (2016)[51]	MACI	32	P, T, BP	4.45	120	Instability: Nm, anatomic risk factors: 10	Realignment: 10, trochleoplasty: 0, soft tissue: 0, non-PF: 6	IKDC: 32.6[b]	Minor: 0, major: 0, failures: 1 (3.1)	Case series, CMS: 80, LOE: 4
von Keudell (2017)[87]	pACI	30	P	4.7	88	Instability: Nm, anatomic risk factors: 18	Realignment: 0, trochleoplasty: 5, soft tissue: 28, non-PF: 23	Mod Cincinnati: 26[b]	Minor: 0, major: 18 (60), failures: 3 (10)	Case series, CMS: 80, LOE: 4
Cvetanovich (2017)[17]	mACI	14	P, T	4	55.2	Instability: Nm, anatomic risk factors: Nm	Realignment: 18, trochleoplasty: 0, soft tissue: 4, non-PF: 0	IKDC: 32.6[b]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 80, LOE: 4
Ebert (2017)[22]	MACI	67	P, T	3	24	Instability: Nm, anatomic risk factors: 3	Realignment: 26, trochleoplasty: 0, soft tissue: 26, non-PF: 0	KOOS ADL: 17.6,[b] KOOS Pain: 21.3,[b] KOOS QoL: 29.5,[b] SF-36 Physical: 10.5[b]	Minor: 4 (6), major: 0, failures: 3 (4.5)	Cohort study, CMS: 71, LOE: 3

(continued)

TABLE 3
(continued)

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Wang (2018)[90]	PJAC	30	P, T, BP	2.14	46	Instability: 10, anatomic risk factors: 10	Realignment: 0, trochleoplasty: 0, soft tissue: 13, non-PF: 4	IKDC: 25.35[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 70, LOE: 4
Berruto (2017)[8]	mACI	13	P, T	5.5	60	Instability: Nm, anatomic risk factors: Nm	Realignment: Nm, trochleoplasty: Nm, soft tissue: Nm, non-PF: Nm	IKDC: 34.8[b]	Minor: 0, major: 0, failures: 1 (7.7)	Prospective cohort, CMS: 61, LOE: 2
Zarkadis (2018)[93]	mACI	73	P, T, BP	4.5	52	Instability: 4, anatomic risk factors: 15	Realignment: 66, trochleoplasty: 0, soft tissue: 3, non-PF: 0	VAS: –3.3[b]	Minor: 0, major: 26 (35.6), failures: 3 (4.1)	Case series, CMS: 67, LOE: 4
38 studies	pACI, mACI, MACI, PJAC	1274	P, T, BP	2.14-12.59	24-153.6	Instability: 136, anatomic risk factors: 377	Realignment: 478, trochleoplasty: 61, soft tissue: 231, non-PF: 83	Outcomes improvement: 30 (83%), no difference: 6 (21%)	Minor: 135 (12.7), major: 95 (9.0), failures: 41 (3.9)	CMS: 73.2 (51-86), LOE: 2 (n = 8), 3 (n = 3), and 4 (n = 27)

[a]ADL, Activities of Daily Living; BP, bipolar lesion; CMS, Coleman Methodology Score; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; LOE, level of evidence; mACI, autologous chondrocyte implantation with membrane; MACI, matrix-induced autologous chondrocyte implantation; Mod Cincinnati, Modified Cincinnati; Nm, not mentioned; P, patellar lesion; pACI, autologous chondrocyte implantation with periosteum; PF, patellofemoral (location not specified); PJAC, particulated juvenile articular cartilage allograft; PRO, patient-reported outcome; QoL, Quality of Life; T, trochlear lesion; VAS, visual analog scale.
[b]Statistically significant finding.
[c]Various chondrocyte techniques were utilized, but the specific generation was not discretely defined.
[d]Preoperative values were not given; therefore, the Δ in PROs could not be calculated, and the included values are postoperative.

found that female patients with lesions in the PF, especially in the patella, had worse results as compared with male patients. For male patients, there were no differences in the results between tibiofemoral and PF compartments.

Meta-analysis Results

Lesion Size. In comparison with the overall pooled lesion size (44 studies; 3.9 cm^2; 95% CI, 3.5-4.3 cm^2), scaffold (2 studies; 2.2 cm^2; 95% CI, 1.8-2.5 cm^2) and OAT (8 studies; 1.5 cm^2; 95% CI, 1.1-1.9 cm^2) had a significantly smaller lesion size ($P < .001$), while chondrocyte cell–based therapy had a significantly larger lesion size (24 studies; 4.7 cm^2; 95% CI, 4.1-5.3 cm^2; $P = .039$) (Appendix Figure A1, available in the online version of this article). Similarly, in comparison with the overall pooled patellar lesion size (30 studies; 3.4 cm^2; 95% CI, 3.1-3.7 cm^2), scaffold had a significantly smaller patellar lesion size (2 studies; 2.2 cm^2; 95% CI, 1.8-2.5 cm^2; $P < .001$), and chondrocyte cell–based therapy had a significantly larger patellar lesion size (15 studies; 4.6 cm^2; 95% CI, 3.9-5.2 cm^2; $P = .002$). However, there was no significant difference observed between any of the groups and the overall pooled trochlear lesion size (11 studies; 4.3 cm^2; 95% CI, 3.4-5.2 cm^2).

Age. Overall weighted mean age (67 studies) was 37.5 years (range, 15-72 years). Of 36 studies reporting distribution, the mean age was 34.4 years (95% CI, 31.2-37.6 years; Q value = 1839.7; $df = 35$; $P < .001$; $I^2 = 98.1\%$). In comparison with the overall distribution, patients receiving bone marrow–based procedures were significantly older (39.7 years; 95% CI, 37.2-42.2 years; $P = .01$).

Follow-up. Overall weighted mean follow-up (67 studies) was 56.1 months (range, 19.3-153.6 months). Of 22 studies reporting distribution, mean follow-up was 49.5 months (95% CI, 43.5-55.5 months; Q value = 22,219.5; $df = 21$; $P < .001$; $I^2 = 99.9\%$). In comparison with the overall distribution, there was a statistically shorter follow-up in the OCA group (36.1 months; 95% CI, 26.2-45.9 months; $P = .026$) and bone marrow–based group (36.4 months; 95% CI, 30.1-42.8 months; $P = .003$).

Associated PF Pathology. The overall pool (29 studies) of instability was 11.9% (95% CI, 0.5%-22.0%; Q value = 196.9; $df = 28$; $P < .001$; $I^2 = 85.8$), and the overall pool (52 studies) of anatomic risk factors was 32.1% (95% CI, 4.4%-41.4%; Q value = 283.8; $df = 51$; $P < .001$; $I^2 = 82.0\%$). OCA had the highest rates of instability (25.9%; 95% CI, 0.0%-95.5%) and anatomic risk factors (43.0%; 95% CI, 0.4%-88.9%). However, there was no significant difference in associated PF pathology between the overall pooled rate and each group, and neither in a pairwise comparison between groups.

Associated Procedures. There was no significant difference observed between any of the groups and the overall pool (52 studies) rate of trochleoplasty (3.3%; 95% CI, 0.4%-5.2%; Q value = 105.8; $df = 51$; $P < .001$; $I^2 = 51.8\%$), rate of soft tissue procedures (52 studies; 10.6%; 95% CI, 0.9%-15.9%; Q value = 234.2; $df = 51$; $P < .001$; $I^2 = 78.2\%$), and rate of non-PF procedures (52 studies; 4.9%; 95% CI, 0.4%-7.6%; Q value = 150.3; $df = 51$; $P < .001$; $I^2 = 66.1\%$). Realignment was most commonly performed in chondrocyte cell–based therapy (37.0%; 95% CI, 7.0%-48.3%) and bone marrow–based therapy (42.1%; 95% CI, 1.4%-78.2%). OCA frequency was 8.4% (95% CI, 0.7%-23.0%). However, the overall pool (52 studies; 27.7%; 95% CI, 3.7%-36.3%; Q value = 286.9; $df = 51$; $P < .001$; $I^2 = 82.2\%$) was significantly different ($P = .025$)

TABLE 4
Results of Patellofemoral Cartilage Restoration: Bone Marrow–Based Therapy With or Without Orthobiologic Augmentation (n = 334, 17.2%)[a]

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Kreuz (2006)[52]	MFx	11	P	2.0	36	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati:, 14.5	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 78, LOE: 4
Kreuz (2006)[52]	MFx	16	T	2.31	36	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	Mod Cincinnati:, 10.6	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 78, LOE: 4
Dhollander (2011)[20]	AMIC-PRP	5	P	2	24	Instability: Nm, anatomic risk factors: Nm	Realignment: 3, trochleoplasty: 0, soft tissue: 1, non-PF: 0	KOOS ADL: 28, KOOS Pain: 28, KOOS QoL: 25, Kujala: 33	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 76, LOE: 4
Wu (2011)[91]	MFx	201	P, T, BP	Nm	50	Instability: 0, anatomic risk factors: 201	Realignment: 0, trochleoplasty: 0, soft tissue: 201, non-PF: 0	Satisfactory postoperative mod. Kujala (>32) in 78.1%[b]	Minor: Nm, major: Nm, failures: Nm	Case series, CMS: 61, LOE: 4
Kusano (2012)[56]	AMIC	20	P	4.4	29.3	Instability: Nm, anatomic risk factors: 18	Realignment: 18, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 23,[b] Lysholm: 27[b]	Minor: 0, major: 9 (45), failures: 0	Case series, CMS: 65, LOE: 4
Petri (2013)[74]	MFx	10	PF	3.0	36	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC postoperative: 50.1,[c] Lysholm postoperative: 59.6,[c] Mod Cincinnati postoperative: 53.8[c]	Minor: Nm, major: Nm, failures: Nm	Retrospective match-pair analysis, CMS: 65, LOE: 4
Teo (2013)[81]	BMAC	3	P	Nm	72	Instability: 0, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 30,[b] Lysholm: 20[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 65, LOE: 4
Dhollander (2014)[19]	AMIC	10	P, T	4.2	24.9	Instability: 0, anatomic risk factors: 0	Realignment: 3, trochleoplasty: 0, soft tissue: 1, non-PF: 0	KOOS ADL: 20.5, KOOS Pain: 20.5, KOOS QoL: 9.6, Kujala: 17.9[b]	Minor: Nm, major: Nm, failures: Nm	Prospective cohort, CMS: 76, LOE: 2
Gobbi (2015)[33]	BMAC	18	P, T, BP	5.54	54.16	Instability: Nm, anatomic risk factors: 5	Realignment: 10, trochleoplasty: 0, soft tissue: 0, non-PF: 2	IKDC: 43.74[b]	Minor: 0, major: 4 (22.2), failures: 0	Prospective comparative study, CMS: 70, LOE: 3
Buda (2019)[11]	BMAC	28	P, T	2.31	48	Instability: Nm, anatomic risk factors: 28	Realignment: 28, trochleoplasty: 0, soft tissue: 0, non-PF: 0	IKDC: 37.0,[b] Kujala: 19[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 75, LOE: 4
Sadlik (2018)[75]	AMIC	12	P	2.46	38	Instability: 1, anatomic risk factors: 4	Realignment: 3, trochleoplasty: 0, soft tissue: 2, non-PF: 0	IKDC: 52.7[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 76, LOE: 4
11 studies	MFx, BMAC, AMIC, AMIC-PRP	334	P, T, BP	2.0-5.54	24-72	Instability: 1, anatomic risk factors: 256	Realignment: 65, trochleoplasty: 0, soft tissue: 205, non-PF: 2	Outcomes improvement: 7 (64%), No difference: 4 (36%)	Minor: 0 (0), major: 13 (12.0), failures: 0 (0)	CMS: 70.7 (61-76), LOE: 2 (n = 1), 3 (n = 1), and 4 (n = 9)

[a]ADL, Activities of Daily Living; AMIC, autologous matrix-induced chondrogenesis; AMIC-PRP, autologous matrix-induced chondrogenesis with platelet-rich plasma; BMAC, bone marrow aspirate concentrate; BP, bipolar lesion; CMS, Coleman Methodology Score; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; LOE, level of evidence; MFx, microfracture; Mod Cincinnati, Modified Cincinnati; Nm, not mentioned; P, patellar lesion; PF, patellofemoral (location not specified); PRO, patient-reported outcome; QoL, Quality of Life; T, trochlear lesion.
[b]Statistically significant finding.
[c]Preoperative values were not given; therefore, the Δ in PROs could not be calculated, and the included values are postoperative.

from only the OAT group (8.2%; 95% CI, 0.2%-30.9%). From pairwise comparison, there was a greater incidence of realignment procedures in the chondrocyte cell–based group than the OAT (P = .027) and OCA (P = .004) groups. There was also a greater incidence of realignment procedures in the bone marrow–based group than the OCA group (P = .041). There was a greater incidence of soft tissue procedures in the OCA group than the bone marrow–based group (P = .049).

Patient-Reported Outcomes. For the meta-regressions of PROs, scores from the IKDC (22 studies and 5 groups), Lysholm (12 studies and 4 groups), and Cincinnati (10 studies and 2 groups) were utilized (Figure 3 and Appendix Figure A2, available online). There were no significant

TABLE 5
Results of Patellofemoral Cartilage Restoration: Scaffold (n = 44, 2.2%)[a]

First Author (Year)	Technique	Knees, n	Lesion Location	Overall Lesion Size, cm^2	Mean Follow-up, mo	Associated Pathology	Associated Procedures	PRO Results, Δ	Complications and Failures, n (%)	Study Design, CMS, and LOE
Joshi (2012)[49]	TruFit	10	P	2.64	24	Instability: Nm, anatomic risk factors: 0	Realignment: 0, trochleoplasty: 0, soft tissue: 0, non-PF: 0	KOOS: 5.2	Minor: 0, major: 0, failures: 7 (70)	Case series, CMS: 76, LOE: 4
Perdisa (2017)[70]	3D-OCS	34	P	2.1	24	Instability: 1, anatomic risk factors: 9	Realignment: 9, trochleoplasty: 0, soft tissue: 2, non-PF: 4	IKDC: 28.1[b]	Minor: 0, major: 0, failures: 0	Case series, CMS: 80, LOE: 4
2 studies	TruFit and 3D-OCS	44	P	2.1-2.64	24	Instability: 1, anatomic risk factors: 9	Realignment: 9, trochleoplasty: 0, soft tissue: 2, non-PF: 4	Outcomes improvement: 1 (50%), no difference: 1 (50%)	Minor: 0 (0), major: 0 (0), failures: 7 (15.9)	CMS: 78 (76-80), LOE: 4 (n = 2)

[a]3D-OCS, 3-dimensional osteochondral scaffold; CMS, Coleman Methodology Score; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; LOE, level of evidence; P, patellar lesion; PF, patellofemoral (location not specified); PRO, patient-reported outcome.
[b]Statistically significant finding.

differences observed between any of the groups and the overall pooled change in IKDC score (30.2; 95% CI, 27.4-32.9) and Lysholm score (25.2; 95% CI, 16.9-33.5). In the Cincinnati score (overall 20.4; 95% CI, 15.9, 24.9), there was a reduced change ($P < .001$) observed after bone marrow–based therapy (4.7; 95% CI, 1.9-7.5) as compared with the overall distribution.

Complications and Failures. No significant differences were observed between any group and the overall (53 studies, 5 groups) pooled rate in minor complication rate (7.6%; 95% CI, 4.7%-11.9%) and major complication rate (8.3%; 95% CI, 5.7%-12.0%). In comparison with the overall pooled failure incidence (6.8%; 95% CI, 4.7%-9.7%), OCA had a significantly greater incidence of failure (22.7%; 95% CI, 14.6%-33.4%) (Figure 4 and Appendix Figure A3, available online).

DISCUSSION

The most important findings of this study were that PF cartilage restoration procedures are reported in a large number of patients, most commonly in the patella. Chondrocyte cell–based therapy was the most common technique utilized, in 65.7% of the studies. Anatomic risk factors were frequently associated (43.5%) as well as PF instability (18.5%). Significant clinical improvement was more often reported in studies of chondrocyte cell–based therapy (83%) and OAT (78%). However, there was no difference in change in IKDC and Lysholm scores in the meta-analysis. Rates of minor and major complications were not different among the techniques; however, failures were higher with OCA. The patella, which is the most frequent location of cartilage lesions in the PF joint,[4,16,46] was also found to be the most common site for cartilage repair procedures (65.7%). This is similar to what Shanmugaraj et al[76] reported on PF cartilage restoration, evaluating 28 studies.

In terms of frequency of techniques, chondrocyte cell–based techniques were performed in 65.7% of the knees, followed by bone marrow–based procedures at 17.2%. This finding is in agreement with what Shanmugaraj et al[76] found. The frequency of chondrocyte cell–based therapy was to be expected, since it was described >20 years ago and has good long-term outcomes in the PF joint.[10,35,63,87] In the bone marrow–based therapy, there has been a clear shift from microfracture, which has been shown to have high failure rates in the PF joint,[55] to enhanced bone marrow therapy, such as autologous matrix-induced chondrogenesis or BMAC implantation.[11,19,20,33,56,75] OCA is another classic procedure but is rarely performed in the PF joint (6.6%), while it is much more common in the femoral condyles.[14,24] This is probably related to the fact that the shapes of the patella and trochlea are more highly variable than the shape of the condyles, which makes matching of the morphology more challenging, particularly with the involvement of the central trochlear groove and median patellar ridge. As a result, focal contained lesions of the patella and trochlea in these regions may be more technically amenable to cell therapy techniques rather than osteochondral procedures.

To interpret clinical outcomes, it is important to understand how variables can interfere in those results. Data are conflicting, but the variables analysis review suggests that age, etiology, location in the patella, and a TTO performed selectively likely do not affect outcomes, while female patients, lesions in the patella, large lesions, and bipolar lesions might have worse results.[††] It is also known that persistent malalignment leads to worse results and that after 10 to 20 years, the outcomes can begin to deteriorate for some patients.[10,73] It is also important to consider the context in which those variables were evaluated—typically, focal cartilage lesions of medium size (3.9 cm^2) in young patients with otherwise healthy knees. Furthermore, some techniques are suitable or used on a narrower range of lesion size (eg, OAT and microfracture in small lesions, ACI and OCA in large lesions), limiting the ability

[††]References 5, 17, 25, 28, 32, 33, 35, 51, 53, 68-70, 73, 82, 84, 90.

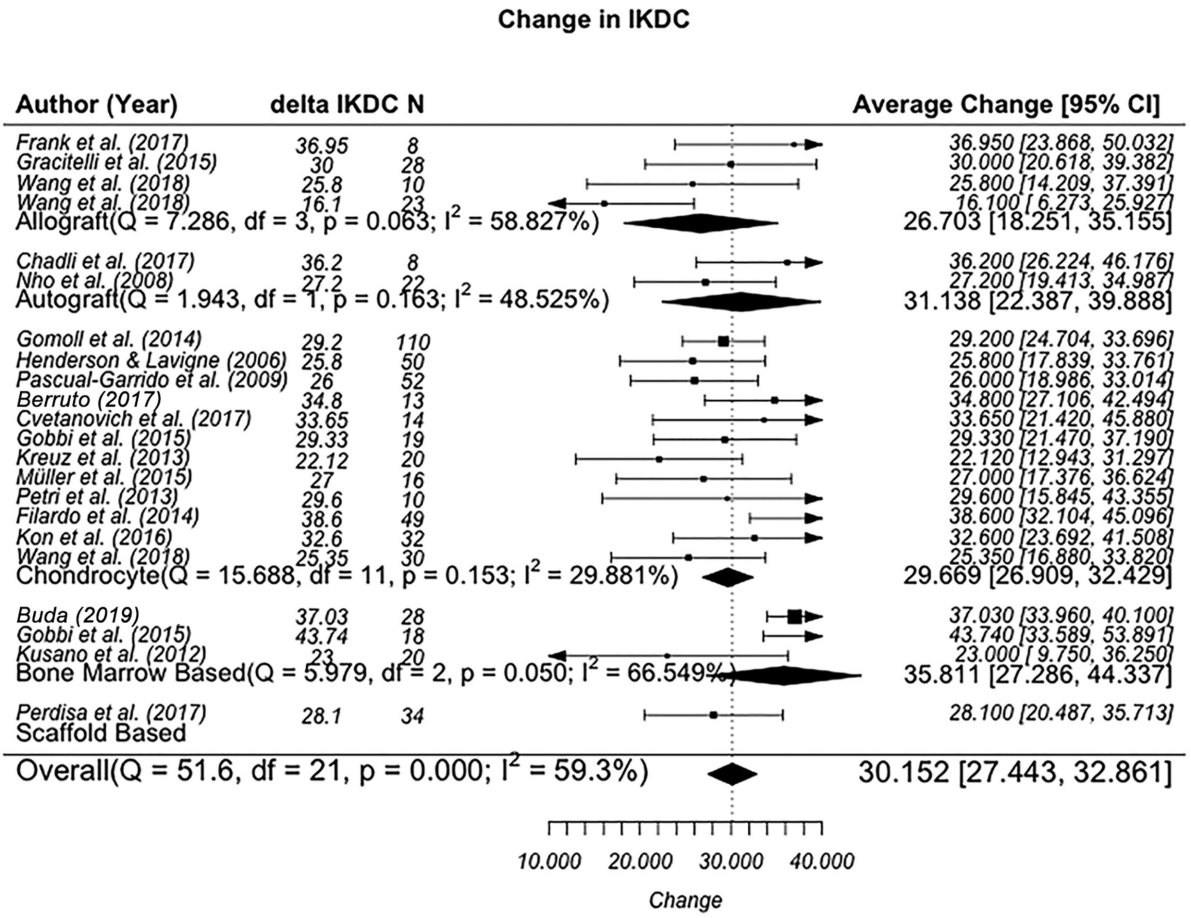

Figure 3. Change in International Knee Documentation Committee (IKDC) score after patellofemoral cartilage restoration procedures. Heterogeneity: Q value = 51.6, df = 21, $P < .001$, I^2 = 59.3%.

to compare results. Thus, for example, age may not have been recognized to influence outcomes within the range of the population most commonly treated (patients <45 years old), but we cannot generalize the information to an older population that has not been studied. In addition, reporting of cartilage lesion characteristics and associated procedures is not ideal in the literature[48] and results in lower-quality studies, and we found that studies were inherently heterogeneous from different operative techniques performed for similar pathology. However, we still have, on average, studies with moderate quality (mean CMS, 71.76) included in this review, and there was no statistical difference among groups to bias our results. Related to those variables, we found the following. The overall lesion size of the chondrocyte cell–based therapy was larger, while OAT and scaffold lesions were smaller. Patients undergoing bone marrow–based procedures were older than the overall distribution. Follow-up was shorter in the OCA and bone marrow–based groups. Instability and anatomic risk factors (11.9% and 32.1%, respectively) were shown to be prevalent and without differences among the groups. This is in accordance with a case-control study by Ambra et al,[3] who found that 75% of patients with deep focal PF cartilage lesions (without PF instability or arthritis) have at least 1 anatomic risk factor. Realignment procedures (including osteotomies) were more frequently performed in the chondrocyte cell–based and bone marrow–based groups than in the OCA group.

We found that outcomes improvement is likely achieved after cartilage repair procedures in the PF joint. More than 70% of the studies on chondrocyte cell–based therapy, OCA, and OAT reported statistically significant improvement in clinical outcomes, while 64% and 50% reported improvement in bone marrow–based therapy and scaffolds, respectively. However, no differences were observed between any group and the overall pooled change in IKDC score (all groups included) or Lysholm score (all but scaffold). In the Cincinnati score (only chondrocyte cell–based vs bone marrow–based therapy), there was a reduced change in bone marrow. Complication rates were relatively low (minor complications, 11.1%; major complications, 8.6%) but still higher than those reported by Gowd et al.[37] In their study evaluating a registry with 15,609 cartilage procedures for lesions in all compartments, the overall complication rate was 2.1% for chondroplasty, 1.4% for microfracture, 1.8% for arthroscopic OAT,

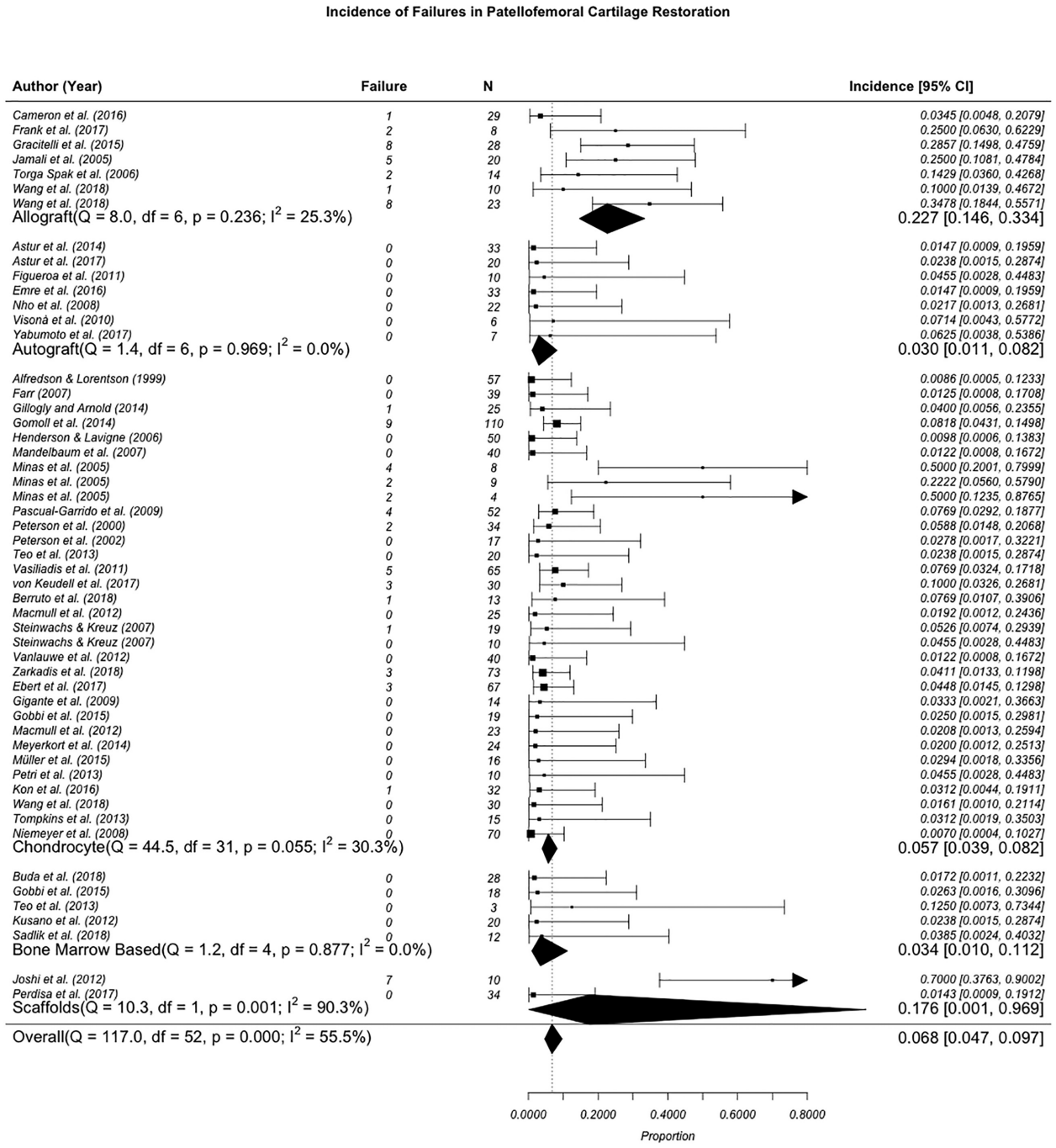

Figure 4. Incidence of failures after patellofemoral cartilage restoration procedures. Heterogeneity: *Q* value = 117.0; *df* = 52; $P < .001$; $I^2 = 55.5\%$.

1.0% for arthroscopic OCA, 1.4% for open OAT, 1.1% for open OCA, and 0.75% for ACI. We found no significant differences in minor and major complication rates, but OCA procedures had a significantly greater incidence of failure. Length of follow-up in studies introduces heterogeneity, as the likelihood of failing treatment will increase with time. The present analysis found OCA and bone marrow–based therapies to have shorter follow-up periods; still, there was an increased incidence of failure with the OCA population. One hypothesis is that the decreased rate of realignment procedures performed in the OCA population—one that has an associated PF pathology similar to that of the population of the other techniques—may be accountable for the higher rate of failures in that group.

Alternatively, the higher failure rate of OCA may reflect its selective use in complex or salvage situations (uncontained lesions, cystic osteochondral defects, failure from prior cartilage restoration procedure). These data may not be clearly reflective of its potential utility as a primary cartilage repair choice in the PF joint for appropriately selected lesions, especially those with significant bone deficiency.

As with all systematic reviews and meta-analyses, the power of the findings is directly proportional to the quality of the studies. The Coleman analysis points to this limitation, as the mean quality was moderate and there were no randomized controlled trials. In addition, the high number of studies reporting zero failures (or not reporting them) increases the concern regarding the quality of the studies. Most of those studies are in the OAT and bone marrow–based therapy groups; alternatively, the smaller lesion size found in the OAT group and the shorter follow-up found in the bone marrow–based therapy can partially explain those zero failure rates. Therefore, those studies should be viewed with caution but do not need to be disregarded. The studies also comprise heterogenic demographics, lesion characteristics, and PF alignment and morphology, which make a direct comparison not possible. Furthermore, some studies did not report on those specific characteristics that can influence outcomes; as such, these data were not available for a direct assessment in the meta-analysis. Those characteristics were, however, reported in the variable analysis section of the systematic review for consideration. In addition, we defined, in the meta-analysis, the mean of many of the variables for each group and were able to infer their possible influences in the results. There is heterogeneity in the reporting of subjective and objective outcomes; therefore, the number of studies included in the meta-analysis for each PRO is small. In addition, the techniques for each procedure and the management of comorbidities have been subtly refined over the reporting years. That is, earlier studies may not be fully representative of current practice, but older and newer studies were weighted equally. Last, as with all systematic reviews, it is possible that relevant articles or patient populations were not identified with our search criteria.

CONCLUSION

Overall, considering the number of procedures performed, the differences in variables, and the clinical outcomes, we believe that, to date, there is more consistent evidence to support the use of chondrocyte cell–based therapy in large lesions and OAT in small lesions as a means to obtain reliable and successful long-term clinical improvement. However, in light of the smaller number of reports of the other techniques, we cannot conclusively comment on their efficacy other than what the raw data demonstrate. That said, it can be concluded that PF cartilage lesions can be successfully addressed with all the techniques evaluated. Going forward, higher-quality studies with greater numbers of participants, universally accepted PROs, and standardized treatment of comorbidities will be essential in creating an algorithm for optimal use of cartilage restoration in the PF compartment.

REFERENCES

1. Alford JW, Cole BJ. Cartilage restoration, part 1: basic science, historical perspective, patient evaluation, and treatment options. *Am J Sports Med*. 2005;33(2):295-306.
2. Alfredson H, Lorentzon R. Superior results with continuous passive motion compared to active motion after periosteal transplantation: a retrospective study of human patella cartilage defect treatment. *Knee Surg Sports Traumatol Arthrosc*. 1999;7(4):232-238.
3. Ambra LF, Hinckel BB, Arendt EA, Farr J, Gomoll AH. Anatomic risk factors for focal cartilage lesions in the patella and trochlea: a case control study. *Am J Sports Med*. 2019;47(10):2444-2453.
4. Aroen A, Loken S, Heir S, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. *Am J Sports Med*. 2004;32(1):211-215.
5. Astur DC, Arliani GG, Binz M, et al. Autologous osteochondral transplantation for treating patellar chondral injuries: evaluation, treatment, and outcomes of a two-year follow-up study. *J Bone Joint Surg Am*. 2014;96(10):816-823.
6. Astur DC, Bernardes A, Castro S, et al. Functional outcomes after patellar autologous osteochondral transplantation. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(10):3084-3091.
7. Bentley G, Biant LC, Vijayan S, Macmull S, Skinner JA, Carrington RW. Minimum ten-year results of a prospective randomised study of autologous chondrocyte implantation versus mosaicplasty for symptomatic articular cartilage lesions of the knee. *J Bone Joint Surg Br*. 2012;94(4):504-509.
8. Berruto M, Ferrua P, Pasqualotto S, et al. Long-term follow-up evaluation of autologous chondrocyte implantation for symptomatic cartilage lesions of the knee: a single-centre prospective study. *Injury*. 2017;48(10):2230-2234.
9. Biggerstaff BJ, Tweedie RL. Incorporating variability in estimates of heterogeneity in the random effects model in meta-analysis. *Stat Med*. 1997;16(7):753-768.
10. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med*. 1994;331(14):889-895.

11. Buda R, Baldassarri M, Perazzo L, Ghinelli D, Pagliazzi G. A useful combination for the treatment of patellofemoral chondral lesions: realignment procedure plus mesenchymal stem cell-retrospective analysis and clinical results at 48 months of follow-up. *Eur J Orthop Surg Traumatol*. 2019;29(2):461-470.
12. Cameron JI, Pulido PA, McCauley JC, Bugbee WD. Osteochondral allograft transplantation of the femoral trochlea. *Am J Sports Med*. 2016;44(3):633-638.
13. Chadli L, Cottalorda J, Delpont M, Mazeau P, Thouvenin Y, Louahem D. Autologous osteochondral mosaicplasty in osteochondritis dissecans of the patella in adolescents. *Int Orthop*. 2017;41(1):197-202.
14. Chahla J, Sweet MC, Okoroha KR, et al. Osteochondral allograft transplantation in the patellofemoral joint: a systematic review. *Am J Sports Med*. 2019;47(12):3009-3018.
15. Cohen M, Amaro JT, De Souza Campos Fernandes R, et al. Osteochondral autologous transplantation for treating chondral lesions in the patella. *Rev Bras Ortop*. 2012;47(3):349-353.
16. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. *Arthroscopy*. 1997;13(4):456-460.
17. Cvetanovich GL, Riboh JC, Tilton AK, Cole BJ. Autologous chondrocyte implantation improves knee-specific functional outcomes and health-related quality of life in adolescent patients. *Am J Sports Med*. 2017;45(1):70-76.
18. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials*. 2015;45(pt A):139-145.
19. Dhollander A, Moens K, Van Der Maas J, Verdonk P, Almqvist KF, Victor J. Treatment of patellofemoral cartilage defects in the knee by autologous matrix-induced chondrogenesis (AMIC). *Acta Orthop Belg*. 2014;80(2):251-259.
20. Dhollander AA, De Neve F, Almqvist KF, et al. Autologous matrix-induced chondrogenesis combined with platelet-rich plasma gel: technical description and a five pilot patients report. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(4):536-542.
21. Ebert JR, Fallon M, Smith A, Janes GC, Wood DJ. Prospective clinical and radiologic evaluation of patellofemoral matrix-induced autologous chondrocyte implantation. *Am J Sports Med*. 2015;43(6):1362-1372.
22. Ebert JR, Schneider A, Fallon M, Wood DJ, Janes GC. A comparison of 2-year outcomes in patients undergoing tibiofemoral or patellofemoral matrix-induced autologous chondrocyte implantation. *Am J Sports Med*. 2017;45(14):3243-3253.
23. Emre TY, Atbasi Z, Demircioglu DT, Uzun M, Kose O. Autologous osteochondral transplantation (mosaicplasty) in articular cartilage defects of the patellofemoral joint: retrospective analysis of 33 cases. *Musculoskelet Surg*. 2017;101(2):133-138.
24. Familiari F, Cinque ME, Chahla J, et al. Clinical outcomes and failure rates of osteochondral allograft transplantation in the knee: a systematic review. *Am J Sports Med*. 2018;46(14):3541-3549.
25. Farr J. Autologous chondrocyte implantation improves patellofemoral cartilage treatment outcomes. *Clin Orthop Relat Res*. 2007; 463:187-194.
26. Farr J, Tabet SK, Margerrison E, Cole BJ. Clinical, radiographic, and histological outcomes after cartilage repair with particulated juvenile articular cartilage: a 2-year prospective study. *Am J Sports Med*. 2014;42(6):1417-1425.
27. Figueroa D, Melean P, Calvo R, Gili F, Zilleruelo N, Vaisman A. Osteochondral autografts in full thickness patella cartilage lesions. *Knee*. 2011;18(4):220-223.
28. Filardo G, Kon E, Andriolo L, Di Martino A, Zaffagnini S, Marcacci M. Treatment of ''patellofemoral'' cartilage lesions with matrix-assisted autologous chondrocyte transplantation: a comparison of patellar and trochlear lesions. *Am J Sports Med*. 2014;42(3):626-634.
29. Filardo G, Kon E, Andriolo L, Di Matteo B, Balboni F, Marcacci M. Clinical profiling in cartilage regeneration: prognostic factors for midterm results of matrix-assisted autologous chondrocyte transplantation. *Am J Sports Med*. 2014;42(4):898-905.
30. Frank RM, Lee S, Levy D, et al. Osteochondral allograft transplantation of the knee: analysis of failures at 5 years. *Am J Sports Med*. 2017;45(4):864-874.
31. Gigante A, Enea D, Greco F, et al. Distal realignment and patellar autologous chondrocyte implantation: mid-term results in a selected population. *Knee Surg Sports Traumatol Arthrosc*. 2009; 17(1):2-10.
32. Gillogly SD, Arnold RM. Autologous chondrocyte implantation and anteromedialization for isolated patellar articular cartilage lesions: 5- to 11-year follow-up. *Am J Sports Med*. 2014;42(4):912-920.
33. Gobbi A, Chaurasia S, Karnatzikos G, Nakamura N. Matrix-induced autologous chondrocyte implantation versus multipotent stem cells for the treatment of large patellofemoral chondral lesions: a nonrandomized prospective trial. *Cartilage*. 2015;6(2):82-97.
34. Gomoll AH, Farr J, Hinckel B. Patellofemoral osteochondral allograft transplantation. *Oper Techn Sports Med*. 2015;23(2):150-156.
35. Gomoll AH, Gillogly SD, Cole BJ, et al. Autologous chondrocyte implantation in the patella: a multicenter experience. *Am J Sports Med*. 2014;42(5):1074-1081.
36. Gomoll AH, Minas T. The quality of healing: articular cartilage. *Wound Repair Regen*. 2014;22(suppl 1):30-38.
37. Gowd AK, Cvetanovich GL, Liu JN, et al. Management of chondral lesions of the knee: analysis of trends and short-term complications using the national surgical quality improvement program database. *Arthroscopy*. 2019;35(1):138-146.
38. Gracitelli GC, Meric G, Pulido PA, Gortz S, De Young AJ, Bugbee WD. Fresh osteochondral allograft transplantation for isolated patellar cartilage injury. *Am J Sports Med*. 2015;43(4):879-884.
39. Gracitelli GC, Meric G, Pulido PA, McCauley JC, Bugbee WD. Osteochondral allograft transplantation for knee lesions after failure of cartilage repair surgery. *Cartilage*. 2015;6(2):98-105.
40. Henderson IJ, Lavigne P. Periosteal autologous chondrocyte implantation for patellar chondral defect in patients with normal and abnormal patellar tracking. *Knee*. 2006;13(4):274-279.
41. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.
42. Hinckel BB, Gomoll AH. Autologous chondrocytes and next-generation matrix-based autologous chondrocyte implantation. *Clin Sports Med*. 2017;36(3):525-548.
43. Hinckel BB, Gomoll AH. Patellofemoral cartilage restoration: indications, techniques, and outcomes of autologous chondrocytes implantation, matrix-induced chondrocyte implantation, and particulated juvenile allograft cartilage. *J Knee Surg*. 2018;31(3): 212-226.
44. Hinckel BB, Gomoll AH, Farr J 2nd. Cartilage restoration in the patellofemoral joint. *Am J Orthop (Belle Mead NJ)*. 2017;46(5): 217-222.
45. Hinckel BB, Sherman SL, Cook JL, Farr J. Current clinical applications for biologic augmentation of cartilage surgery. In: *Let's Discuss: Biologics in Orthopaedics*. Rosemont, IL: AAOS; 2017:1-31.
46. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. *Arthroscopy*. 2002;18(7):730-734.
47. Jamali AA, Emmerson BC, Chung C, Convery FR, Bugbee WD. Fresh osteochondral allografts: results in the patellofemoral joint. *Clin Orthop Relat Res*. 2005;437:176-185.
48. Jones KJ, Sheppard WL, Arshi A, Hinckel BB, Sherman SL. Articular cartilage lesion characteristic reporting is highly variable in clinical outcomes studies of the knee. *Cartilage*. 2019;10(3):299-304.
49. Joshi N, Reverte-Vinaixa M, Diaz-Ferreiro EW, Dominguez-Oronoz R. Synthetic resorbable scaffolds for the treatment of isolated patellofemoral cartilage defects in young patients: magnetic resonance imaging and clinical evaluation. *Am J Sports Med*. 2012;40(6): 1289-1295.
50. Jungmann PM, Gersing AS, Baumann F, et al. Cartilage repair surgery prevents progression of knee degeneration. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(9):3001-3013.

51. Kon E, Filardo G, Gobbi A, et al. Long-term results after hyaluronan-based MACT for the treatment of cartilage lesions of the patellofemoral joint. *Am J Sports Med*. 2016;44(3):602-608.
52. Kreuz PC, Erggelet C, Steinwachs MR, et al. Is microfracture of chondral defects in the knee associated with different results in patients aged 40 years or younger? *Arthroscopy*. 2006;22(11):1180-1186.
53. Kreuz PC, Muller S, von Keudell A, et al. Influence of sex on the outcome of autologous chondrocyte implantation in chondral defects of the knee. *Am J Sports Med*. 2013;41(7):1541-1548.
54. Kreuz PC, Steinwachs M, Erggelet C, et al. Classification of graft hypertrophy after autologous chondrocyte implantation of full-thickness chondral defects in the knee. *Osteoarthritis Cartilage*. 2007;15(12):1339-1347.
55. Kreuz PC, Steinwachs MR, Erggelet C, et al. Results after microfracture of full-thickness chondral defects in different compartments in the knee. *Osteoarthritis Cartilage*. 2006;14(11):1119-1125.
56. Kusano T, Jakob RP, Gautier E, Magnussen RA, Hoogewoud H, Jacobi M. Treatment of isolated chondral and osteochondral defects in the knee by autologous matrix-induced chondrogenesis (AMIC). *Knee Surg Sports Traumatol Arthrosc*. 2012;20(10):2109-2115.
57. Lefkoe TP, Trafton PG, Ehrlich MG, et al. An experimental model of femoral condylar defect leading to osteoarthrosis. *J Orthop Trauma*. 1993;7(5):458-467.
58. Macmull S, Jaiswal PK, Bentley G, Skinner JA, Carrington RW, Briggs TW. The role of autologous chondrocyte implantation in the treatment of symptomatic chondromalacia patellae. *Int Orthop*. 2012; 36(7):1371-1377.
59. Mandelbaum B, Browne JE, Fu F, et al. Treatment outcomes of autologous chondrocyte implantation for full-thickness articular cartilage defects of the trochlea. *Am J Sports Med*. 2007;35(6):915-921.
60. Messner K, Maletius W. The long-term prognosis for severe damage to weight-bearing cartilage in the knee: a 14-year clinical and radiographic follow-up in 28 young athletes. *Acta Orthop Scand*. 1996;67(2):165-168.
61. Meyerkort D, Ebert JR, Ackland TR, et al. Matrix-induced autologous chondrocyte implantation (MACI) for chondral defects in the patellofemoral joint. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(10): 2522-2530.
62. Minas T, Bryant T. The role of autologous chondrocyte implantation in the patellofemoral joint. *Clin Orthop Relat Res*. 2005;436:30-39.
63. Minas T, Von Keudell A, Bryant T, Gomoll AH. The John Insall Award: a minimum 10-year outcome study of autologous chondrocyte implantation. *Clin Orthop Relat Res*. 2014;472(1):41-51.
64. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009;62(10):1006-1012.
65. Müller S, Hirschmuller A, Erggelet C, Beckmann NA, Kreuz PC. Significantly worse isokinetic hamstring-quadriceps ratio in patellofemoral compared to condylar defects 4 years after autologous chondrocyte implantation. *Knee Surg Sports Traumatol Arthrosc*. 2015;23(8):2151-2158.
66. Nho SJ, Foo LF, Green DM, et al. Magnetic resonance imaging and clinical evaluation of patellar resurfacing with press-fit osteochondral autograft plugs. *Am J Sports Med*. 2008;36(6):1101-1109.
67. Niemeyer P, Porichis S, Steinwachs M, et al. Long-term outcomes after first-generation autologous chondrocyte implantation for cartilage defects of the knee. *Am J Sports Med*. 2014;42(1):150-157.
68. Niemeyer P, Steinwachs M, Erggelet C, et al. Autologous chondrocyte implantation for the treatment of retropatellar cartilage defects: clinical results referred to defect localisation. *Arch Orthop Trauma Surg*. 2008;128(11):1223-1231.
69. Pascual-Garrido C, Slabaugh MA, L'Heureux DR, Friel NA, Cole BJ. Recommendations and treatment outcomes for patellofemoral articular cartilage defects with autologous chondrocyte implantation: prospective evaluation at average 4-year follow-up. *Am J Sports Med*. 2009;37(suppl 1):33S-41S.
70. Perdisa F, Filardo G, Sessa A, et al. One-step treatment for patellar cartilage defects with a cell-free osteochondral scaffold. *Am J Sports Med*. 2017;45(7):1581-1588.
71. Peterson L, Brittberg M, Kiviranta I, Akerlund EL, Lindahl A. Autologous chondrocyte transplantation: biomechanics and long-term durability. *Am J Sports Med*. 2002;30(1):2-12.
72. Peterson L, Minas T, Brittberg M, Nilsson A, Sjögren-Jansson E, Lindahl A. Two-to 9-year outcome after autologous chondrocyte transplantation of the knee. *Clin Orthop Relat Res*. 2000;374:212-234.
73. Peterson L, Vasiliadis HS, Brittberg M, Lindahl A. Autologous chondrocyte implantation: a long-term follow-up. *Am J Sports Med*. 2010;38(6):1117-1124.
74. Petri M, Broese M, Simon A, et al. CaReS (MACT) versus microfracture in treating symptomatic patellofemoral cartilage defects: a retrospective matched-pair analysis. *J Orthop Sci*. 2013;18(1):38-44.
75. Sadlik B, Matlak A, Blasiak A, Klon W, Puszkarz M, Whyte GP. Arthroscopic cartilage lesion preparation in the human cadaveric knee using a curette technique demonstrates clinically relevant histologic variation. *Arthroscopy*. 2018;34(7):2179-2188.
76. Shanmugaraj A, Coughlin RP, Kuper GN, et al. Changing trends in the use of cartilage restoration techniques for the patellofemoral joint: a systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2019;23(3):854-867.
77. Sidik K, Jonkman JN. A note on variance estimation in random effects meta-regression. *J Biopharm Stat*. 2005;15(5):823-838.
78. Song F, Gilbody S. Bias in meta-analysis detected by a simple, graphical test: increase in studies of publication bias coincided with increasing use of meta-analysis. *BMJ*. 1998;316(7129):471.
79. Steinwachs M, Kreuz PC. Autologous chondrocyte implantation in chondral defects of the knee with a type I/III collagen membrane: a prospective study with a 3-year follow-up. *Arthroscopy*. 2007;23(4):381-387.
80. Stijnen T, Hamza TH, Ozdemir P. Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. *Stat Med*. 2010;29(29): 3046-3067.
81. Teo BJ, Buhary K, Tai BC, Hui JH. Cell-based therapy improves function in adolescents and young adults with patellar osteochondritis dissecans. *Clin Orthop Relat Res*. 2013;471(4):1152-1158.
82. Tompkins M, Hamann JC, Diduch DR, et al. Preliminary results of a novel single-stage cartilage restoration technique: particulated juvenile articular cartilage allograft for chondral defects of the patella. *Arthroscopy*. 2013;29(10):1661-1670.
83. Torga Spak R, Teitge RA. Fresh osteochondral allografts for patellofemoral arthritis: long-term followup. *Clin Orthop Relat Res*. 2006; 444:193-200.
84. Vanlauwe JJ, Claes T, Van Assche D, Bellemans J, Luyten FP. Characterized chondrocyte implantation in the patellofemoral joint: an up to 4-year follow-up of a prospective cohort of 38 patients. *Am J Sports Med*. 2012;40(8):1799-1807.
85. Vasiliadis HS, Lindahl A, Georgoulis AD, Peterson L. Malalignment and cartilage lesions in the patellofemoral joint treated with autologous chondrocyte implantation. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(3):452-457.
86. Visonà E, Chouteau J, Aldegheri R, Fessy MH, Moyen B. Patella osteochondritis dissecans end stage: the osteochondral mosaicplasty option. *Orthop Traumatol Surg Res*. 2010;96(5):543-548.
87. von Keudell A, Han R, Bryant T, Minas T. Autologous chondrocyte implantation to isolated patella cartilage defects. *Cartilage*. 2017; 8(2):146-154.
88. Wang D, Kalia V, Eliasberg CD, et al. Osteochondral allograft transplantation of the knee in patients aged 40 years and older. *Am J Sports Med*. 2018;46(3):581-589.
89. Wang D, Rebolledo BJ, Dare DM, et al. Osteochondral allograft transplantation of the knee in patients with an elevated body mass index [published online February 9, 2018]. *Cartilage*. doi:10.1177/1947603518754630

90. Wang T, Belkin NS, Burge AJ, et al. Patellofemoral cartilage lesions treated with particulated juvenile allograft cartilage: a prospective study with minimum 2-year clinical and magnetic resonance imaging outcomes. *Arthroscopy*. 2018;34(5):1498-1505.
91. Wu CC. Combined lateral retinacular release with drilling chondroplasty for treatment of patellofemoral osteoarthritis associated with patellar malalignment in elderly patients. *Knee*. 2011; 18(1):24-29.
92. Yabumoto H, Nakagawa Y, Mukai S, Saji T. Osteochondral autograft transplantation for isolated patellofemoral osteoarthritis. *Knee*. 2017;24(6):1498-1503.
93. Zarkadis NJ, Belmont PJ Jr, Zachilli MA, et al. Autologous chondrocyte implantation and tibial tubercle osteotomy for patellofemoral chondral defects: improved pain relief and occupational outcomes among US Army servicemembers. *Am J Sports Med*. 2018;46(13): 3198-3208.