Autologous Chondrocyte Implantation in the Patella: A Multicenter Experience

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Autologous Chondrocyte Implantation in the Patella

A Multicenter Experience

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Background: Cartilage defects in the patella are common, and a subset of patients does not respond to nonoperative measures. While most cartilage repair techniques have demonstrated good outcomes in the femoral condyles, the patellofemoral compartment poses special challenges.

Hypothesis: Repair of patellar cartilage defects with autologous chondrocyte implantation (ACI) will provide lasting improvements in pain and function.

Study Design: Case series; Level of evidence, 4.

Methods: Patients were treated at 1 of 4 participating cartilage repair centers with ACI for cartilage defects in the patella; bipolar (patella + trochlea) defects were included as well. All patients were followed prospectively for at least 4 years with multiple patient-reported outcome instruments, including the International Knee Documentation Committee, Short Form–12, modified Cincinnati Rating Scale, Western Ontario and McMaster Universities Osteoarthritis Index, and Knee Society scores. Treatment failure was defined as structural failure of the graft combined with pain requiring revision surgery.

Results: A total of 110 patients were available for analysis. As a group, they experienced both statistically significant and clinically important improvements in pain and function in all physical outcome scales. The International Knee Documentation Committee improved from 40 ± 14 preoperatively to 69 ± 20 at the last follow-up; the Cincinnati Rating Scale, from 3.2 ± 1.2 to 6.2 ± 1.8; and the Western Ontario and McMaster Universities Osteoarthritis Index, from 50 ± 22 to 29 ± 22 (all $P < .0001$). Ninety-two percent of patients stated that they would choose to undergo ACI again, and 86% rated their knees as good or excellent at the time of final follow-up. Nine patients (8%) were considered treatment failures, and 16% reported that their knees were not improved.

Conclusion: Cartilage repair in the patellofemoral joint is arguably not without its challenges. Autologous chondrocyte implantation remains off-label in the patella, a fact that needs to be discussed with prospective patients during the informed consent process. However, when performed with attention to patellofemoral biomechanics, self-rated subjective good and excellent outcomes can be achieved in more than 80% of patients treated with ACI, even in a patient population with large and frequently bipolar defects such as the one presented in this study. However, final functional scores, although significantly improved, still reflected residual disability in this challenging group of patients.

Keywords: autologous chondrocyte implantation; cartilage repair; patellofemoral; multicenter study

Cartilage defects are common, being present in more than 50% of patients undergoing knee arthroscopy. The articular surface of the patella is affected in 11% to 36% of cases, making it, along with the medial femoral condyle, one of the most frequently affected locations in the knee joint.[8,18] The cause of these defects is multifactorial, including chronic repetitive microtrauma and distinct macrotrauma, most commonly patellar dislocation, which is associated with chondral defects in up to 95% of patients.[30] Left untreated, cartilage defects worsen over time, although the speed of progression cannot be predicted for the individual patient.[6,9] Even isolated cartilage defects can cause morbidity comparable with advanced osteoarthritis.[15] Cartilage defects are often seen in younger patients in their most productive years, spurring increased interest in interventions that can improve pain and function. However, cartilage repair in the patella is challenging. Most procedures have demonstrated less satisfactory outcomes and increased failure rates when compared with the femoral condyles,[14,20,22] and additional research is needed to better define indications and results of cartilage repair in the patellofemoral compartment.

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We present a large multicenter review of patients treated with autologous chondrocyte implantation (ACI) for cartilage defects located in the patella. Due to its relevance for clinical practice, patients with bipolar defects (additional trochlear defect) were included as well. Patients with additional grafts outside the patellofemoral compartment were excluded.

MATERIALS AND METHODS

Patient Population

Patients treated at 4 participating centers specializing in cartilage repair were eligible for inclusion in the study. All 4 participating surgeons had extensive experience with ACI, each having performed more than 200 procedures. Each center maintained an institutional review board–approved database to prospectively follow all patients undergoing cartilage repair; the first of these databases was established in 1997. The databases were queried, and all patients treated with ACI for patellar defects with at least 4 years of follow-up were included in this study. While a trochlear graft was acceptable, patients with defects outside the patellofemoral compartment (eg, femoral condyle or tibial defects) were excluded.

Indications

Autologous chondrocyte implantation is indicated for the treatment of medium to large chondral defects with no or shallow associated osseous deficits. In the United States, ACI is approved by the Food and Drug Administration (FDA) for use in the femur (medial and lateral femoral condyles; trochlea), but it is also routinely used to treat patellar defects in an off-label fashion. Specifically, in the context of this study, patients were indicated for ACI if they presented with persistent disabling anterior knee pain unresponsive to nonoperative measures, including at least 3 to 6 months of supervised physical therapy. Radiographs were obtained to rule out advanced patellofemoral arthritis; patients with more than 50% of joint space narrowing were not deemed candidates for biological resurfacing. Magnetic resonance imaging scans were used to further delineate the exact location and size of cartilage defects, as well as to assess the condition of the subchondral bone. If patients were deemed potential candidates for ACI, an arthroscopy was scheduled to evaluate the joint for other articular comorbidities, perform a chondroplasty, and obtain a cartilage biopsy specimen if the indication for ACI was confirmed.

Surgical Technique

Autologous Chondrocyte Implantation. The original technique of ACI was developed more than 15 years ago[5] and has been used in the United States to treat more than 10,000 patients since its approval by the FDA in 1997. The procedure was performed as described previously in greater detail.[25] Briefly, chondrocytes were expanded in cell culture from a cartilage biopsy specimen harvested arthroscopically. After a variable interval in cryopreservation, the cells were expanded again in preparation for implantation, then shipped to the respective centers. The cartilage defects were prepared by removing all degenerated tissue to create stable shoulders of healthy cartilage. A periosteal patch was harvested from the proximal tibia and microsutured to the surrounding cartilage to create a watertight space. In case of uncontained defects, sutures were placed through the adjacent synovium or through transosseous drill holes. The suture lines were sealed with fibrin glue to ensure a watertight seal. The defects were then injected with the chondrocyte suspension at a density of greater than 1 million cells per square centimeter. While the ideal cell density for reimplantation is controversial, in current practice reimplantation of approximately 12 million cells is recommended for an average size lesion of 4 to 6 cm^2.

Concurrent Procedures. Tibial tubercle (tuberosity) osteotomy (TTO) is frequently considered a concurrent procedure for patellofemoral cartilage repair. The indications for TTO were history of patellar instability (dislocation or subluxation), patellar maltracking on physical examination, and abnormal tibial tuberosity–trochlear groove (TT-TG) distance (>15 mm).[1] Large uncontained or bipolar defects were also treated with TTO, even in the absence of patellar maltracking, to reduce patellofemoral contact forces. An anteromedialization technique was utilized, aiming to anteriorize the tibial tubercle by approximately 10 to 15 mm and normalizing the TT-TG distance without overmedialization. In cases of normal preoperative TT-TG distance, the osteotomy was modified to produce a vertical (steep) cut for almost exclusive anteriorization without medialization.[2,37]

Lateral release was performed, either with the classic full-thickness technique or through titrated lateral lengthening, in all cases of decreased patellar mobility.[32]

Postoperative Rehabilitation

The rehabilitative protocol progressed in stages.

Stage I (weeks 1-6 after surgery) included the patient's use of a locked brace for ambulation, continuous passive motion for 6 to 8 hours per day, and range of motion and

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isometric muscle exercises. Weightbearing was restricted for 6 weeks to touchdown when a TTO was performed concurrently. Patients with isolated ACI were allowed weightbearing as tolerated in full extension. Generally, continuous passive motion was started at 0° to 40° and advanced by 5° per day. Very large and bipolar defects were advanced more slowly to limit shear forces on the graft.

Stage II (7-12 weeks) included active range of motion exercises, gradually progressing to full range of motion and full weightbearing.

Stage III (12+ weeks) continued to advance functional activities. Open chain knee extension and stair climbing was discouraged for 6 months. Patients were restricted from inline impact activities (running) for 12 to 18 months and from cutting sports for at least 18 months.

Treatment Failures

Patients were considered to have failed treatment if they were diagnosed by magnetic resonance imaging and/or arthroscopy with structural failure of the ACI graft in conjunction with pain requiring revision surgery. Repeat arthroscopy for debridement of graft hypertrophy or lysis of adhesions was not considered a treatment failure.

Functional Outcomes

Patients were followed prospectively with questionnaires to assess function, activity level, and satisfaction with the procedure. Each center entered data into separate, institution-specific databases approved by their respective institutional review boards. Patients completed questionnaires, including an overall well-being and quality-of-life survey (Short Form–12),[42] 2 knee-specific instruments (Knee Society score; International Knee Documentation Committee [IKDC]),[17,19] and 1 sports activity–based instrument (modified Cincinnati Rating Scale),[31] as well as a generalized, nonspecific arthritis score (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]).[3] Also, they were asked to answer questions pertaining to their satisfaction with the procedure. Questionnaires were answered independently by the patients without physician interaction, mostly at home, and were mailed in.

Statistical Methods

Data were collected preoperatively, then at yearly intervals. Patient-reported outcomes were analyzed at 2 points: preoperatively and at latest follow-up. Student *t* tests were used to examine differences from baseline within each group. The level of statistical significance was set at $P < .05$.

Subanalyses were performed per the number of defects (unipolar vs bipolar), defect size, defect location on the patella (medial, lateral, panpatellar), patient sex, containment of the defect, and whether a concurrent tibial tuberosity osteotomy had been performed. Analysis of variance tests were performed to determine differences among groups, followed by Tukey post hoc tests to examine for significance between groups. The level of statistical significance was set at $P < .05$.

RESULTS

Demographics

A total of 110 patients fulfilled the inclusion criteria. An additional 23 patients were lost to follow-up (follow-up rate, 83%). There were 64 females and 46 males with an average age of 33 years at the time of the index procedure (range, 15-55 years; SD, 10.1 years). Patients were followed after surgery for an average of 90 months (range 48-192 months; SD, 31.7 months). There were 59 right and 51 left knees treated; no patients with bilateral procedures fulfilled the inclusion criteria. Twenty patients (18%) were covered by workers' compensation insurance. On average, patients reported symptoms before ACI for 3 years (range, 2-144 months; SD, 35 months) and had undergone an average of 1.2 prior surgeries (range, 0-12; SD, 1.7), excluding the cartilage biopsy specimen for ACI. The 2 most common prior procedures were chondroplasty and lateral release.

Patient populations at the 4 centers showed only mild heterogeneity (Table 1). Statistical examination demonstrated a significant difference for only 2 comparisons: between the 2 centers with the largest and smallest average defect size and with 1 center performing TTO more frequently than the others. No other statistically significant differences were seen for patient age, sex, containment, or polarity.

Defect Characteristics

Every patient had a patellar defect as specified in the inclusion criteria, with an average defect size of 5.4 cm^2 (range, 1-13.2 cm^2; SD, 2.7 cm^2). Thirty patients (27%) had bipolar disease with an additional trochlear defect, with an average size of 4.5 cm^2 (range, 1-13 cm^2; SD, 2.8 cm^2). Based on the Pidoriano/Fulkerson classification[35] for the location of patellar defects, there were 12 distal (11%; type I), 3 lateral (3%; type II), 16 medial (15%; type III), and 79 central/panpatellar defects (72%; type IV). The majority of defects were contained: 82 (75%) of patellar defects and 26 (87%) of trochlear defects were circumferentially shouldered by healthy cartilage.

Concurrent Procedures

The most common concurrent procedure was a TTO, generally of the Fulkerson (anteromedialization) type, in 75 (69%) patients. A trochleoplasty for dysplasia was performed in 5 (5%) patients, lateral release in 45 (41%), vastus medialis advancement in 22 (20%), and medial patellofemoral ligament reconstruction in 1 patient.

Failures

Nine patients were considered treatment failures and were revised with total (n = 4) or partial knee replacement

TABLE 1
Center-Specific Demographics[a]

Center	No. of Patients	Age, y	Female, %	Patellar Defect Size,[a] cm^2	TTO, %	Contained, %	Unipolar, %
1	30	31.4	60	6.95 ± 2.67	97	77	83
2	20	31.1	50	3.75 ± 2.04	55	85	95
3	45	35.3	60	5.00 ± 2.49	60	69	56
4	15	30.3	60	5.36 ± 2.41	53	67	73

[a]Mean ± SD. TTO, tibial tubercle osteotomy.

TABLE 2
Functional Outcome Scores[a]

Outcome Measure	No. of Patients (%)	Mean Score		*P* Value
		Preoperative	Last Follow-up	
SF-12				
PCS	89 (81)	38.6	44.1	.001
MCS	89 (81)	49.7	53.5	.1
IKDC	65 (60)	40.2	69.4	<.0001
Modified Cincinnati	85 (78)	3.2	6.2	<.0001
WOMAC	44 (40)	50.4	28.6	<.0001
KSS				
Knee	44 (40)	61.8	85.2	<.0001
Function	44 (40)	58.5	72.7	<.0001

[a]IKDC, International Knee Documentation Committee; KSS, Knee Society score; MCS, Mental Component Subscale; PCS, Physical Component Subscale; SF-12, Short Form–12; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

(n = 4); 1 patient declined further surgical management. These failures were included in the analyses.

Patient-Reported Outcomes

Since the start of the databases more than 15 years ago, new patient-reported outcome instruments have become available—for example, the IKDC. These were added once their validity had been established. The start date for these questionnaires differed among the institutions; therefore, not all patients answered the same battery of questionnaires (Table 2). Within each center, however, the completion rate of questionnaires was >90%. Overall, the Short Form–12 Physical Component Subscale demonstrated an increase from 38.6 to 44.1 ($P = .001$); the Mental Component Subscale increased insignificantly from 49.7 to 53.5 ($P = .1$). The IKDC score increased from 40.2 to 69.4 ($P < .0001$); 86% and 74% of patients demonstrated more than 10 and 20 points of improvement, respectively—both are threshold values considered to exceed minimal clinically important differences (MCIDs).[7] The modified Cincinnati score (2-10 scale) increased from 3.2 to 6.2 ($P < .0001$). The WOMAC score improved from 50.4 to 28.6 (lower numbers reflect better function); 75% of patients exceeded a commonly accepted threshold for MCIDs, with more than a 26% improvement in WOMAC from baseline.[43] The Knee Society knee score increased from 61.8 to 85.2 and the Knee Society function score, from 58.5 to 72.7 ($P < .0001$).

Of the 93 patients asked to rate their knee, 84% stated that they felt improvement at the time of final follow-up; 86% rated their knee function as good or excellent; and 92% would choose to undergo ACI again.

Subanalyses

Subanalyses were performed to investigate specific differences in polarity (bi- vs unipolar), containment (contained vs uncontained; patellar defects only), concomitant tibial tuberosity transfer (yes vs no), patellar defect location (lateral, medial, panpatellar), defect size, and sex (male vs female) (see the Appendix, available online at http://ajsm.sagepub.com/supplemental). None of the differences among subgroups reached statistical significance (all $P > .05$).

DISCUSSION

We present an analysis of prospectively collected outcome data from 4 high-volume cartilage repair centers. A total of 110 patients with cartilage defects of the patella were evaluated at a minimum of 4 years after treatment with ACI. Patients experienced both statistically significant and clinically important improvements in pain and function in all physical outcome scales. Ninety-two percent of patients stated that they would choose to undergo ACI again, and 84% rated their knee as improved at the time

of final follow-up. Nine patients (8%) were considered treatment failures.

The field of cartilage repair continues to evolve, and additional studies are required to help refine indications, define outcomes, and better manage expectations. Patellofemoral pain in particular remains a difficult-to-manage entity that primarily should be approached nonoperatively. A select group of patients with patellofemoral pain, however, presents with treatment-resistant symptoms from cartilage defects that can be considered for cartilage repair. None of the established procedures have shown results that are equal to or better than outcomes after treatment for femoral condyle defects, demonstrating the need for additional studies investigating cartilage repair in the patella.

Microfracture has shown only transient improvement in this location, with worsening symptoms after 18 to 36 months.[22] The use of synthetic plugs (TruFit CB; Smith & Nephew, Andover, Massachusetts, USA) is associated with high failure rates and the formation of large subchondral cysts, requiring revision surgery in 70%.[21] The use of osteochondral autograft transfer (OAT) in the patellofemoral compartment has demonstrated inconsistent outcomes: Hangody and Fules[14] reported results that were acceptable, but lesser than in the femoral condyle. Bentley et al,[4] however, had almost universal failure of OAT in the patella. One factor considered to be potentially involved in failure of OAT is the mismatch in cartilage thickness between the donor and recipient sites, which results in a step-off at the osteochondral junction with the potential for subsequent cyst formation.[41] Osteochondral allograft transplantation could potentially solve this issue, since homologous grafts could be utilized (patella to patella, rather than peripheral trochlea to patella). Jamali et al[20] investigated the use of osteochondral allografts in the PF compartment and reported only 60% good and excellent results. Torga Spak[38] presented a long-term follow-up of 14 patellofemoral allografts, with a survival of 57% at an average of 10 years.

Autologous chondrocyte implantation has been used for almost 20 years for the treatment of full-thickness cartilage defects of the knee. It has demonstrated successful outcomes in approximately 80% of patients when used in the femoral condyles or trochlea.[24,34,44] The first report on its use in the patella, in 1994, showed disappointing results of only 28% good or excellent outcomes.[5] Since then, increased understanding of patellofemoral joint kinematics has led to refined indications and techniques, as well as to more aggressive correction of patellar maltracking, resulting in drastically improved outcomes with success in more than 70% to 80% of patients, nearly matching outcomes in the femur.[10,11,16,23,26,33] However, even with these recent improvements, the use of ACI in the patellofemoral joint, specifically in the patella, remains somewhat controversial, not insignificantly owing to its FDA off-label status when used in this location. To provide a historical perspective, the FDA did not regulate cell therapy at the time when ACI was first introduced to the United States in 1995, but it subsequently developed a policy on cell therapy in 1996-1997. As ACI was already in clinical use, the FDA determined indications for use according to the results of the Brittberg et al study,[5] choosing to include only the femoral condyles and trochlea during their review in 1997.

Our results are comparable with those of other studies of patellofemoral ACI. Gobbi et al[13] demonstrated an increase in IKDC from 46 to 70 at 5 years, almost identical to our results (40 and 69, respectively). The Niemeyer et al[29] report on 70 patients showed an IKDC of 62 at an average of 3 years after surgery. Henderson and Lavigne[16] described IKDC values of 85 in patellar ACI with TTO and 61 in isolated ACI. However, their groups contained a significant number of patients with lateral facet defects, which have been described to be most sensitive to realignment osteotomy.[29] To refine indications for ACI, several studies investigated factors with the potential to influence outcomes, suggesting better results in males, in unipolar defects, and with concurrent TTO.[16,28,39] We therefore performed subanalyses to investigate potential effects of defect location on the patella, patient sex, defect containment, whether defects were uni- or bipolar, and whether a concurrent TTO was performed. None of the subanalyses demonstrated statistically significant differences among groups in our patient population. More than 70% of patients had defects that were contained, unipolar, and panpatellar and underwent concurrent TTO. This left only small control groups, likely resulting in insufficient power to detect subtle differences. In terms of defect location, only 14% of patients were treated for isolated defects in the lateral or inferior aspects of the patella, which are considered prime indications for isolated TTO with almost 90% success rate. Conversely, the remaining 86% of defects were located in the medial facet, panpatellar, or associated with trochlear defects; isolated TTO has demonstrated good and excellent results in only 55%, 20%, or even 0% of defects in these locations, respectively.[35] In comparison, treatment of these challenging defect locations with ACI (with or without TTO) led to self-assessed subjective good and excellent results in 86% of our patients, a remarkable improvement over isolated TTO.

Our subanalysis demonstrated no significant differences between patients treated with and without concurrent TTO. However, this should not be interpreted as TTO never being beneficial. One previous study reported that patients treated with ACI had better outcomes if they also underwent TTO.[16] A potential explanation for this discrepancy in findings could be related to the higher number of lateral and inferior defects in that study (approximately 35%, vs 14% in the present study). Defects in these locations would be expected to respond more dramatically to a TTO, resulting in a larger difference between groups treated with and without TTO. Conversely, the preponderance of medial and central defects in our study would minimize these differences. Furthermore, the rate of TTO in our study was quite high (68%), resulting in a correspondingly smaller control group and decreasing power to detect small differences. Our results are comparable with another publication that reported no significant differences between a group with ACI where patellar maltracking had been corrected through TTO and a group without maltracking that had undergone isolated ACI.[40] Similarly,

additional subgroup analyses did not find any statistically significant differences in patient-reported outcomes among groups in terms of defect location, size, containment, and patient gender. We performed a post hoc power analysis, which demonstrated the need for more than 500 patients in each subgroup to reach a power of 80%, based on the demonstrated average group scores. The differences in these group averages are smaller than what has been determined to be clinically meaningful; therefore, even though a larger sample size could reach statistical significance, patients would be unlikely to perceive a meaningful difference in their function.

Our study shares the limitations inherent to all nonrandomized investigations. ACI is a rare procedure, with only approximately 1500 cases performed annually in the United States, in comparison with approximately 600,000 knee replacement procedures. Furthermore, pathologic disorders vary substantially among patients, with cartilage defects of different sizes, locations, and numbers, as well as comorbidities such as patellar maltracking, malalignment, meniscal and ligamentous deficiencies, and variability in body mass index. As such, identifying and enrolling sufficiently uniform patients for randomized trials is challenging, as evidenced by the recent termination of 2 large phase 2 FDA trials for new cartilage repair implants, owing to difficulty with enrollment (Zimmer DeNovo ET [Clinicaltrials.gov NCT01400607]; DePuy Mitek CAIS [Clinicaltrials.gov NCT00881023]). Specifically for patellofemoral cartilage repair studies, additional complexity is created by the lack of a reasonable procedure to act as control for randomization: techniques such as microfracture and OAT are considered problematic in the patella, with some authors reporting only transient pain relief and high failure rates.[4,22] Debridement alone could be considered a control; however, patients are understandably reluctant to agree to palliative treatment options that provide only transient improvement, especially when considering that delaying cartilage repair has been associated with compromised outcomes.[39] In an attempt to address some of the limitations inherent to single-surgeon case series, we pooled data from 4 large cartilage repair centers to increase numbers and minimize the influence of surgeon-specific variations in indications, surgical techniques, and patient populations. Data were collected prospectively, with each center having defined follow-up protocols for cartilage repair patients at the start of its database, enrolling initial patients more than a decade ago.

Nine patients (8%) were considered treatment failures based on revision with arthroplasty (one of these patients was indicated for but declined further surgical treatment); these patients were included in the outcomes analysis. Clearly, the definition of what constitutes failure of a procedure is complex and controversial. We chose an objective criterion: revision with knee replacement. More subjective endpoints can be considered, and we included one that might offer the most important summary statement of a patient's experience with the procedure and its outcomes—the question of whether a patient would choose to undergo the procedure again if faced with the same decision. Ninety-two percent of patients answered this question in the affirmative. Remarkably, even among the 9 patients deemed treatment failures, only 1 would not undergo ACI again; the other 8 considered the time worthwhile that ACI delayed treatment with arthroplasty—on average, 7 years. Other studies have demonstrated similar numbers of revision procedures, with a substantial percentage being revision cartilage procedures.[10,12,24,27,28,36,44] However, all patients in our study were revised with partial or total knee arthroplasty, rather than repeat cartilage repair. This potentially reflects the complex and unforgiving biomechanical environment of the patellofemoral joint, which does not lend itself to repeat biological repair. This finding should be considered in lieu of making treatment decisions in this location to maximize successful outcomes—for example, to aggressively pursue correction of maltracking through distal realignment at the time of cartilage repair.

In summary, patients improved significantly in physical functioning from baseline after treatment of large patellar cartilage defects with ACI. They reported improved knee function and high satisfaction with the procedure, with more than 90% of patients willing to undergo ACI again. Across multiple outcome instruments, statistically significant improvements were seen in knee function. More important, these improvements exceeded thresholds termed MCIDs. Validation studies have defined these thresholds as levels of improvement that patients rate as bringing meaningful improvement in function. The MCID has been defined for the IKDC, although 2 different thresholds are being used by various authors. With the commonly accepted 10-point threshold, 86% of patients improved, while 74% fulfilled the stricter 20-point requirement. With a 26% improvement in the WOMAC score as an MCID threshold, 75% of patients experienced meaningful improvements in their function. According to the modified Cincinnati scale, patients had significant limitations in activities of daily living and were unable to participate in sports before surgery (preoperative modified Cincinnati score, 3.2). Postoperatively, patients reported good function with daily activities and the ability to participate in sports with some limitations (postoperative modified Cincinnati score, 6.2). The effect of such activity improvement can hardly be overstated, especially in a patient population averaging only 33 years of age with young families and at the beginning of their careers. However, it is important to point out during the informed consent process that even though patients can expect above-mentioned significant improvements in pain and function, their knees will likely not be completely normal and some limitations will remain.

In conclusion, 8% of patients were classified as treatment failures, but even among this group, a majority would undergo treatment with ACI again. Subanalyses did not demonstrate any significant differences in outcome based on defect location, polarity, sex, or containment, potentially because of small control groups. We also could not demonstrate any differences based on whether patients had undergone concurrent TTO or not. This should not be interpreted as TTO not being beneficial but rather as a reflection of aggressive correction of patellar maltracking in the majority of cases, essentially comparing a "normal" to a "normalized" biomechanical environment.

Cartilage repair in the patellofemoral joint is arguably not without its challenges. ACI remains off-label in the patella, a fact that needs to be discussed with prospective patients during the informed consent process. However, when it is performed with attention to patellofemoral biomechanics, self-related subjective good or excellent outcomes can be achieved in more than 80% of patients treated with ACI, even in a patient population with large and frequently bipolar defects, such as the one presented in this study.

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