# Autologous Chondrocyte Implantation and Osteochondral Allograft Transplantation Render Comparable Outcomes in the Setting of Failed Marrow Stimulation

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**Background:** Marrow stimulation techniques (MSTs) such as subchondral drilling and microfracture are often chosen as first-line treatment options for symptomatic cartilage defects of the knee. When an MST fails, many cartilage restoration techniques are employed, including autologous chondrocyte implantation (ACI) and osteochondral allograft (OCA). However, a few series in the literature suggest that ACI after a failed MST results in inferior outcomes as compared with primary ACI.

**Purpose/Hypothesis:** The purpose of this study was (1) to evaluate the clinical outcomes of ACI and OCA after a failed MST (secondary ACI and OCA) and compare them with the outcomes of primary ACI and OCA and (2) to compare clinical outcomes of secondary ACI and secondary OCA for refractory lesions involving the femoral condyle. The hypotheses were as follows: (1) secondary ACI will render inferior functional outcomes and an increased clinical failure rate as compared with primary ACI, (2) secondary OCA will render comparable results to primary OCA, and (3) secondary OCA will render superior outcomes to secondary ACI.

**Study Design:** Cohort study; Level of evidence, 3.

**Methods:** Patients were retrospectively identified who underwent ACI and OCA for symptomatic chondral lesions of the knee refractory to a previous MST. Age-, sex-, and body mass index–matched groups of patients undergoing primary ACI and OCA were used as controls. Postoperative data were prospectively collected using several subjective scoring systems (Tegner, Lysholm, International Knee Documentation Committee, Knee injury and Osteoarthritis Outcome Score, 12-Item Short Form Health Survey). Groups were compared with regard to patient-reported outcomes, subjective satisfaction, clinical failure rate, and reoperation. Student *t* tests were used for continuous data, and chi-square tests were performed for categorical data.

**Results:** A total of 359 patients were examined: 92 patients undergoing secondary ACI, 100 primary ACI, 88 secondary OCA, and 79 primary OCA. The mean patient age was 30.3 years (range, 14.9-49.9 years) at the time of ACI and 35.4 (range, 15-54.5) at the time of OCA. There was no difference between the primary and secondary groups with regard to postoperative functional scores, subjective satisfaction, reoperation rate, and clinical failure rate.

**Conclusion:** ACI and OCA are both viable treatment options for chondral defects of the knee, even in the setting of a failed MST. Secondary ACI renders functional outcomes, subjective satisfaction, and reoperation and failure rates comparable with primary ACI and secondary OCA.

**Keywords:** knee; articular cartilage; allografts

Full-thickness cartilage defects of the knee have very limited capacity for spontaneous healing and can cause significant disability as a result of pain, swelling, and mechanical symptoms. When nonsurgical treatment measures fail, surgical intervention is often required for symptom relief. In general, surgical options are grouped into 3 categories: palliative (arthroscopic debridement and lavage), reparative (marrow stimulation techniques [MSTs]), and restorative (autologous chondrocyte implantation [ACI], osteochondral autograft transfer system, osteochondral allograft [OCA], and juvenile cartilage). With such a broad array of options, selecting the appropriate surgical technique can be challenging and remains a source of controversy. Traditional algorithms generally favor a graduated surgical plan favoring less aggressive measures (debridement and MST) as first-line treatment. MSTs

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have demonstrated good results, with improvement in knee function in 70% to 95% of patients.[5,8,9,16-18] Nonetheless, some authors have suggested that an MST may compromise outcomes of ACI owing to violation of underlying subchondral bone.[11,13] These authors, in turn, have advocated for first-line treatment with ACI in higher-risk lesions and osteochondral grafting in the setting of a failed MST. The purpose of this study was to compare clinical outcomes, subjective satisfaction, reoperation, and clinical failure rates (1) between patients who underwent primary ACI and secondary ACI, (2) between patients who underwent primary OCA and secondary OCA and (3) between patients who underwent secondary ACI and those who underwent secondary OCA to the femoral condyle.

## METHODS

### Patient Selection

The study protocol was approved by the medical center's institutional review board. This cohort study, based on prospectively collected data, was conducted to assess differences in patient-reported outcomes (PROs), subjective satisfaction, reoperation rate, and clinical failure rate between patients undergoing ACI and OCA with and without a prior MST, including either subchondral drilling or microfracture. The indication for ACI and OCA was the presence of a symptomatic, full-thickness (grade IV) chondral defect involving the patella, trochlea, or femoral condyles that was refractory to prior microfracture or subchondral drilling. The decision to undergo OCA or ACI after MTS was dictated by the senior surgeon (B.J.C.) and institutional preference: patients treated before 2005 generally underwent ACI, while those after 2005 underwent OCA.

### Outcome Assessment

Patient data were collected, including age, sex, body mass index, lesion sites, lesion size, number of lesions, and concomitant procedures performed. PROs were assessed with several validated knee outcome questionnaires. The surveys included the following outcome scales: Tegner, Lysholm, International Knee Documentation Committee (IKDC), Knee injury and Osteoarthritis Outcome Score (KOOS), and 12-Item Short Form Health Survey. The KOOS is subdivided and scored in 5 categories: Pain, Quality of Life, Activities of Daily Living, Sports and Recreation, and Symptoms. Subjective satisfaction was assessed by asking patients if they were completely satisfied, mostly satisfied, somewhat satisfied, or unsatisfied. Failure was defined as persistent or recurrent symptoms and evidence of graft delamination or grade IV chondrosis involving a significant portion of the graft site on second-look arthroscopy, a revision cartilage restoration procedure (ACI, microfracture, OCA, Denovo NT), or a prosthetic replacement.

Comparisons were made (1) between patients undergoing secondary ACI and OCA and those undergoing primary ACI and OCA, respectively, and (2) between patients undergoing secondary ACI and those undergoing secondary OCA for lesions involving the femoral condyle. Because patients undergoing OCA to the femoral condyle tended to be older than those undergoing ACI, an age-, sex-, and body mass index (BMI)–matched cohort of patients undergoing OCA was selected for the purposes of comparison. Matching was manually performed in Microsoft Excel and confirmed with Student *t* tests.

### Operative Technique and Rehabilitation

ACI was performed in a 2-stage fashion as originally described.[1,18] The senior surgeon transitioned from using periosteum to collagen I/III membrane in October 2007, so 146 patients underwent ACI with a periosteal patch, and 46 underwent ACI with a collagen I/III membrane. Similarly, OCA transplantation was performed in a manner that has been broadly described.[4,6,7] A small vastus-sparing medial or lateral arthrotomy was used for lesions involving the medial or lateral femoral condyle, respectively.

Postoperatively, patients adhered to our institution's rehabilitation protocol. Immediately after surgery, the patient's leg was placed in a hinged knee brace locked in full extension for the first 2 weeks. Patients were permitted to unlock the brace during exercise and to use a continuous passive motion machine for 4 to 6 hours daily. For grafts to the patellofemoral joint, immediate full weightbearing was permitted with the brace in full extension (unless a tibial tubercle osteotomy was performed). For grafts to the femoral condyles, weightbearing was restricted to nonweightbearing for 6 weeks and advanced to full weightbearing by 8 weeks. Braces were discontinued at 2 weeks if patients were capable of a straight leg raise without an extension lag. Beginning at 8 weeks, therapy focused on core strengthening, balance training, unilateral

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stance activities, and closed kinetic-chain exercises. At 12 weeks, patients were advanced to elliptical, bike, or pool activities. Patients were generally returned to impact and sport-specific activity around postoperative 8 months.

### Statistical Analysis

Statistics were performed with SPSS (v 23; IBM Inc). Unpaired Student *t* tests were performed to assess for differences between primary ACI and OCA groups and secondary ACI and OCA groups with regard to patient characteristics and PROs. A paired Student *t* test was used to assess for improvements in questionnaire measures within the study group between presurgery and final follow-up. Chi-square testing was performed to detect differences in categorical data, including patient satisfaction, rate of reoperation, and rate of clinical failure. Kaplan-Meier survivorship analysis was performed to assess for differences in failure rates between study groups. Cox regression analysis was performed to isolate patient characteristics correlated with clinical failure. Statistical significance was set at $P < .05$. No a priori power analysis was performed, and as many patients as possible undergoing secondary ACI or OCA were recruited. A post hoc power analysis was performed to determine if the study was sufficiently powered to determine a difference in clinical failure rate.

## RESULTS

### Patient and Lesion Characteristics

Between October 1998 and December 2011, 92 patients at one institution with a history of an MST underwent ACI to the patella, trochlea, medial femoral condyle, or lateral femoral condyle. The mean (± SD) age was 30.3 ± 9.0 years (range, 14.9-49.9 years). The group contained 52 men and 40 women (57% men). The mean BMI was 26.5 ± 5.1. The study group was well-matched to a control group of 100 patients who underwent primary ACI with regard to age, sex, BMI, workers' compensation status, and follow-up duration (Table 1). The groups were also well-matched with regard to number of chondral lesions, lesion location, primary lesion area, total lesion area, and concomitant procedures performed (Table 2). The mean interval between the MST and ACI was 21.2 ± 16.0 months (range, 5-88 months).

Between January 2002 and January 2014, 88 patients at one institution with a prior MST underwent OCA to the medial femoral condyle or lateral femoral condyle. The mean patient age was 35.4 ± 10.7 years (range, 15-54.5 years). The group contained 45 men and 43 women (51% men). The mean BMI was 27.0 ± 4.7. The study group was well-matched to a control group of 79 patients who underwent primary OCA with regard to age, sex, BMI, workers' compensation status, and follow-up duration (Table 3). Study and control groups were well-matched with regard to lesion location, graft size, and proportion undergoing realignment osteotomy (Table 4). Of note, patients undergoing primary OCA were more likely than the secondary OCA cohort to undergo concomitant meniscal allograft transplantation (50% vs 18%; $P$ = .003). The mean duration from the MST to OCA was 30.0 ± 46.3 months (range, 3-288 months).

A total of 46 patients underwent secondary ACI to a femoral condyle lesion. Although 88 patients underwent OCA to a primary lesion involving the femoral condyle refractory to an MST, this group was narrowed to 59 patients to generate an age-, sex-, and BMI-matched cohort for the purposes of comparison with ACI (Table 5). While there was a shorter interval between an MST and cartilage restoration in the ACI cohort than in the OCA cohort (18.5 ± 18.6 vs 35.0 ± 54.5 months; $P$ = .04), the ACI and OCA groups were well-matched with regard to lesion location, the size of the primary lesion, and concomitant procedures performed (Table 6).

TABLE 1
Characteristics of Patients Undergoing ACI After a Marrow Stimulation Technique and Those Undergoing Primary ACI[a]

| | Secondary ACI (n = 92) | Primary ACI (n = 100) | *P* Value |
|---|---|---|---|
| Age, y | 30.3 ± 9.0 | 30.4 ± 9.4 | .92 |
| Sex: male | 52 (57) | 50 (50) | .51 |
| Body mass index, kg/m$^2$ | 26.5 ± 5.1 | 26.4 ± 4.9 | .85 |
| Workers' compensation | 23 (25) | 24 (25) | .87 |
| Follow-up, mo | 47.3 ± 23.6 | 43.5 ± 20.9 | .35 |

[a]Values are presented as mean ± SD or n (%). ACI, autologous chondrocyte implantation.

### Outcome Assessment: Secondary vs Primary ACI

Mean preoperative compliance for all PROs was 81% in the secondary ACI group and 84% in the primary ACI group. Mean postoperative compliance was 76% and 88% across all surveys for the secondary and primary ACI groups, respectively. Mean duration of follow-up was 47.3 ± 23.6 months and 43.5 ± 20.9 months for the secondary and primary ACI groups, respectively. Eighteen patients in the secondary ACI group had >5-year follow-up, while 14 patients had >5-year follow-up in the primary ACI group. The secondary ACI group demonstrated more preoperative disability than the primary ACI group with regard to Tegner activity level (3.4 vs 4.4; $P$ = .049); however, the groups were well- matched with regard to all other subjective questionnaire measures, including the Lysholm, IKDC, KOOS (Pain, Quality of Life, Activities of Daily Living, Sports and Recreation, and Symptoms scores), and 12-Item Short Form Health Survey (physical and mental) (Figure 1). At minimum 2-year follow-up, there was no difference between the primary and secondary ACI groups with regard to any of the subjective questionnaire measures. Among 86 patients in the secondary ACI group who completed the satisfaction survey, 33 were completely

TABLE 2
Lesion Characteristics and Concomitant Procedures Performed Among Patients Undergoing ACI After a Marrow Stimulation Technique and Primary ACI[a]

| | Secondary ACI (n = 92) | Primary ACI (n = 100) | *P* Value |
|---|---|---|---|
| No. of defects, 1:2:3:4, n | 73:17:1:1 | 77:19:4:0 | NA |
| Proportion with 1 lesion, % | 79 | 77 | .69 |
| Location, patellofemoral:tibiofemoral:both, % | 38:48:14 | 48:36:16 | NA |
| Primary lesion location, TR:PT:MFC:LFC, n | 25:19:38:10 | 28:25:29:18 | NA |
| Primary lesion area, mm$^2$, mean | 417 | 402 | .62 |
| Total defect area, mm$^2$, mean | 506 | 504 | .96 |
| Concomitant procedures, n (%) | | | |
| Patellar anteromedialization | 31 (34) | 31 (31) | .69 |
| Realignment osteotomy, HTO:DFO | 5:1 (7) | 1:2 (3) | .25 |
| Meniscal transplantation, MMT:LMT | 5:3 (9) | 2:7 (9) | .94 |
| Collagen membrane:periosteal patch, n (% [collagen]) | 21:71 (23) | 25:75 (25) | .72 |

[a]ACI, autologous chondrocyte implantation; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; LFC, lateral femoral condyle; LMT, lateral meniscal transplant; MFC, medial femoral condyle; MMT, medial meniscal transplant; NA, not applicable; PT, patella; TR, trochlea.

TABLE 3
Characteristics of Patients Undergoing OCA After a Marrow Stimulation Technique and Those Undergoing Primary OCA[a]

| | Secondary OCA (n = 88) | Primary OCA (n = 79) | *P* Value |
|---|---|---|---|
| Age, y | 35.4 ± 10.7 | 32.5 ± 10.4 | .07 |
| Sex: male | 45 (51) | 40 (51) | .96 |
| Body mass index, kg/m$^2$ | 27.0 ± 4.7 | 26.1 ± 5.8 | .32 |
| Workers' compensation | 16 (18) | 15 (19) | .90 |
| Follow-up, mo | 44.4 ± 27.3 | 43.5 ± 20.9 | .35 |

[a]Values are presented as mean ± SD or n (%). OCA, osteochondral allograft.

TABLE 4
Lesion Characteristics and Concomitant Procedures Performed Among Patients Undergoing OCA after a Marrow Stimulation Technique and Primary OCA[a]

| | Secondary OCA (n = 88) | Primary OCA (n = 79) | *P* Value |
|---|---|---|---|
| Location, MFC:LFC:both (% [MFC]) | 61:24:3 (69) | 44:32:3 (56) | NA |
| Bicondylar, n (%) | 3 (3.4) | 3 (3.8) | .90 |
| Lesion area, mean, mm$^2$ | 396 | 496 | .22 |
| Graft diameter, mean, mm | 19.9 | 21.3 | .12 |
| Concomitant procedure, n (%) | | | |
| Realignment osteotomy, HTO:DFO | 8:3 (13) | 9:3 (15) | .64 |
| Meniscal transplantation, MMT:LMT | 9:10 (22) | 23:17 (50) | .003 |

[a]DFO, distal femoral osteotomy; HTO, high tibial osteotomy; LFC, lateral femoral condyle; LMT, lateral meniscal transplant; MFC, medial femoral condyle; MMT, medial meniscal transplant; NA, not applicable; OCA, osteochondral allograft.

TABLE 5
Age-, Sex-, and BMI-Matched Cohort of Patients Undergoing OCA and ACI After a Marrow Stimulation Technique to the Femoral Condyle[a]

| | Secondary ACI (n = 46) | Secondary OCA (n = 59) | *P* Value |
|---|---|---|---|
| Age, y | 28.7 ± 10.4 | 29.7 ± 9.1 | .58 |
| Male:female (% [male]) | 25:21 (54) | 31:28 (53) | .90 |
| BMI, kg/m$^2$ | 26.0 ± 4.9 | 26.7 ± 4.7 | .47 |
| Workers' compensation | 9 (20) | 8 (14) | .45 |
| Follow-up, mo | 54.2 ± 24.4 | 54.7 ± 32.4 | .94 |

[a]Values are presented as mean ± SD or n (%). ACI, autologous chondrocyte implantation; BMI, body mass index; OCA, osteochondral allograft.

TABLE 6
Technical Characteristics of Age-, Sex-, and BMI-Matched Cohort of Patients Undergoing OCA and ACI After an MST to the Femoral Condyle[a]

| | Secondary ACI (n = 46) | Secondary OCA (n = 59) | *P* Value |
|---|---|---|---|
| Lesion location, MFC:LFC:both (% [MFC]) | 35:10:1 (76) | 37:20:2 (63) | .34 |
| Primary lesion size, mm$^2$ | 410 ± 200 | 389 ± 216 | .60 |
| Interval MST to restoration, mo | 18.5 ± 18.6 | 35.0 ± 54.5 | .04 |
| Concomitant procedure | | | |
| Realignment osteotomy, HTO:DFO | 3:2 (11) | 6:3 (15) | .54 |
| Meniscal transplantation, MMT:LMT | 5:3 (17) | 9:6 (25) | .38 |

[a]Values are presented as n (%) or mean ± SD. ACI, autologous chondrocyte implantation; BMI, body mass index; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; LFC, lateral femoral condyle; LMT, lateral meniscal transplant; MFC, medial femoral condyle; MMT, medial meniscal transplant; MST, marrow stimulation technique; OCA, osteochondral allograft.

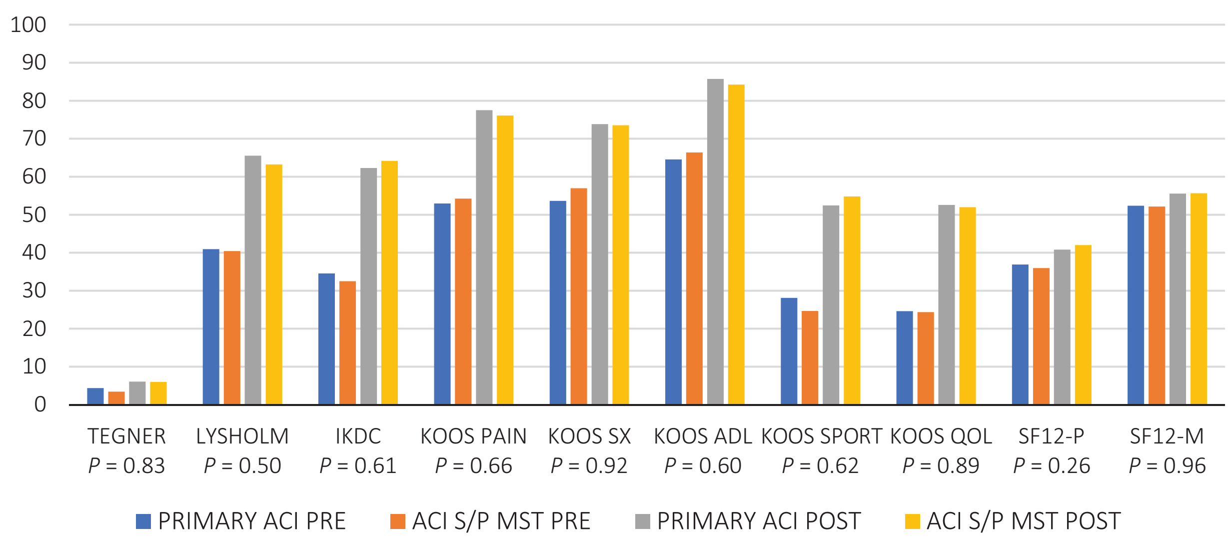


**Figure 1.** Pre- and postoperative functional scores in patients with autologous chondrocyte implantation (ACI) with and without prior marrow stimulation. *P* values refer to significance of difference between postoperative groups. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; MST, marrow stimulation technique; POST, postoperative; PRE, preoperative; QOL, Quality of Life; SF-12-M, 12-Item Short Form Health Survey (mental); SF-12-P, 12-Item Short Form Health Survey (physical); S/P, status post; SX, Symptoms.

satisfied, 33 mostly satisfied, 11 somewhat satisfied, and 9 unsatisfied. In the primary ACI group, 40 were completely satisfied, 24 mostly satisfied, 16 somewhat satisfied, and 12 unsatisfied. There was no difference between the primary and secondary ACI groups with regard to the proportion of patients who were mostly or completely satisfied (77% vs 70%, *P* = .46) (Figure 2).

In the secondary ACI group, 13% of knees (11 of 86) experienced clinical failure (3 total knee arthroplasties [TKAs], 4 OCAs, 1 revision ACI, 1 microfracture, 1 Denovo NT, and 1 graft delamination on second-look arthroscopy) as compared with 8% (7 of 92) in the primary ACI group (1 TKA, 1 unicompartmental knee arthroplasty [UKA], 2 OCAs, and 3 with grade IV chondrosis on second-look arthroscopy) (*P* = .15). Among all patients, the failure rate was 17% (8 of 47) for the workers' compensation subgroup and 6% (9 of 145) for the non–workers' compensation subgroup (*P* = .02). Reoperation was performed in 31% of secondary ACI cases (10 for graft failure and 17 for other reasons) and 30% of primary ACI cases (7 for graft failure and 21 for other reasons) (*P* = .84) (Figure 3). Other reasons for reoperation included mild pain, locking, or catching. Types of reoperations for other reasons included debridement, lysis of adhesions, plica excision, hardware removal, and suprapatellar pouch release. Reoperation for graft failure was performed at a mean 29.2 ± 27.2 months after ACI, and reoperation for other reasons was performed at a mean 31.6 ± 12.5 months postoperatively.

## Outcome Assessment: Secondary OCA vs Primary OCA

Mean preoperative compliance for all PROs was 65% in the secondary OCA group and 57% in the primary OCA group. Postoperative PRO and follow-up data were available for

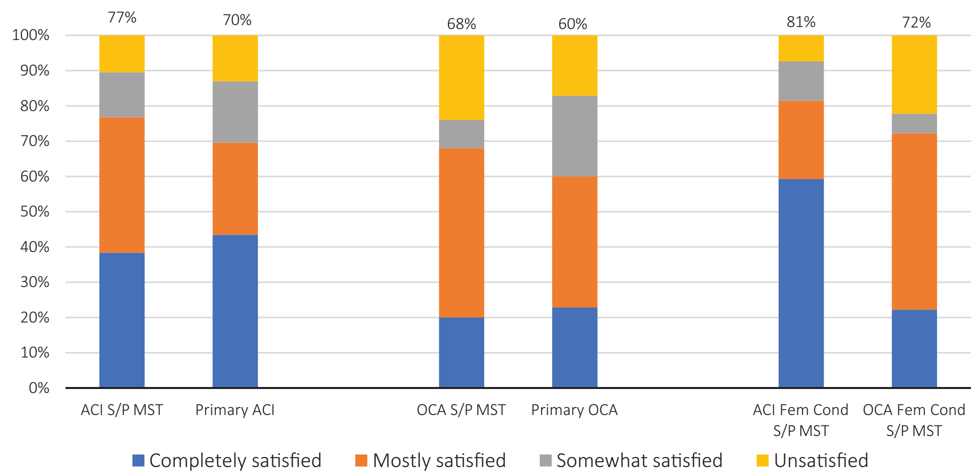


**Figure 2.** Comparison of subjective patient satisfaction between the study and control groups. Labels indicate percentage of patients who were mostly or completely satisfied with the outcome of the procedure. ACI, autologous chondrocyte implantation; Fem Cond, femoral condyle; MST, marrow stimulation technique; OCA, osteochondral allograft; S/P, status post.

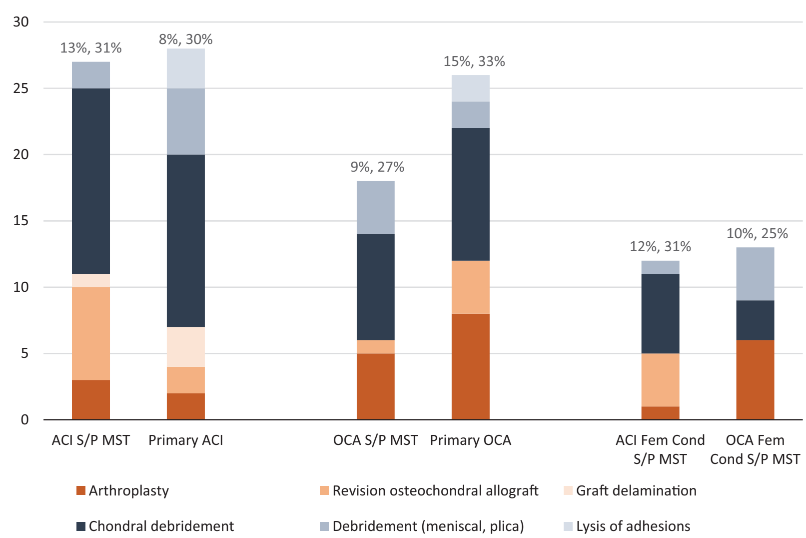


**Figure 3.** Comparison of revision and reoperation rates between the study and control groups. Labels indicate rate of clinical failure and reoperation. ACI, autologous chondrocyte implantation; Fem Cond, femoral condyle; MST, marrow stimulation technique; OCA, osteochondral allograft; S/P, status post.

a mean 74% and 96% across all surveys for the secondary and primary OCA groups, respectively. Mean duration of follow-up was 43.5 ± 20.9 months. Twenty patients in the secondary OCA group extended beyond 5 years, while 27 patients in the primary OCA group had >5-year follow-up. There was no difference between the groups with regard to preoperative or minimum 2-year follow-up PROs (Figure 4). There was no difference between the secondary and primary OCA groups with regard to the proportion who were mostly or completely satisfied (68% vs 60%; $P$ = .70) (Figure 2). In the secondary OCA group, 9% (6 of 70) experienced clinical failure (3 TKAs, 2 UKAs, and 1 revision OCAs) as compared with 15% (12 of 79) in the primary OCA group (6 TKAs, 2 UKAs, 4 revision OCAs) ($P$ = .34). Reoperation was performed in 27% of secondary OCA cases (7 for graft failure and 12 for other reasons) and 33% of primary OCA cases (12 for graft failure and 14 for other reasons) ($P$ = .44) (Figure 3). Reoperation for graft failure was performed at a mean 36.2 months after ACI, and reoperation for other reasons was performed at a mean 18.4 months postoperatively. Similar to the ACI group, other reasons for surgery in the secondary and primary OCA groups included mild pain, locking, or catching.

## Outcome Assessment: Secondary ACI vs Secondary OCA

For patients undergoing secondary ACI and OCA to the femoral condyle, minimum 2-year follow-up surveys were

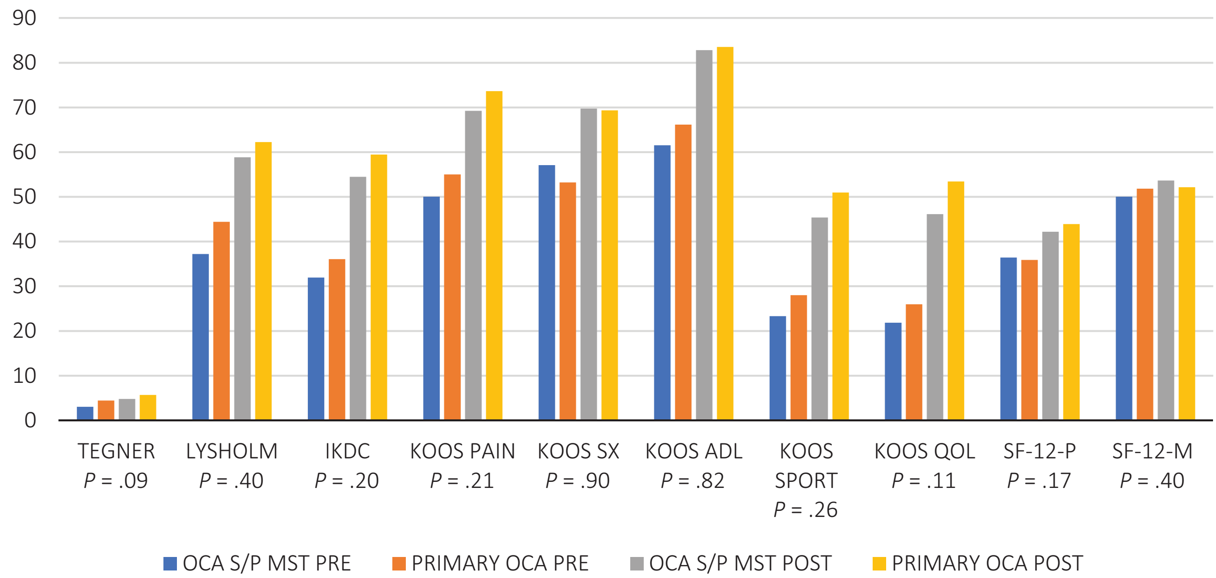


**Figure 4.** Pre- and postoperative patient-reported outcomes in patients with osteochondral allograft (OCA) with and without prior marrow stimulation. *P* values refer to significance of difference between postoperative groups. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; MST, marrow stimulation technique; POST, postoperative; PRE, preoperative; QOL, Quality of Life; SF-12-M, 12-Item Short Form Health Survey (mental); SF-12-P, 12-Item Short Form Health Survey (physical); S/P, status post; SX, Symptoms.

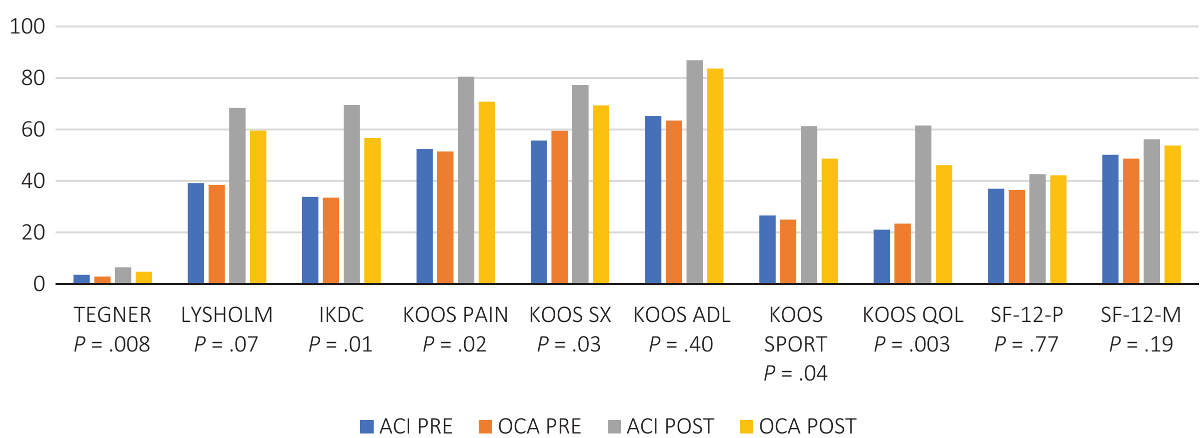


**Figure 5.** Pre- and postoperative functional scores in patients undergoing autologous chondrocyte implantation (ACI) or osteochondral allograft (OCA) to the femoral condyle after a failed MST. *P* values refer to significance of difference between postoperative groups. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MST, marrow stimulation technique; POST, postoperative; PRE, preoperative; QOL, Quality of Life; SF-12-M, 12-Item Short Form Health Survey (mental); SF-12-P, 12-Item Short Form Health Survey (physical); SX, Symptoms.

available for 91% (42 of 46) and 76% (45 of 59) of patients, respectively. There was no difference between the groups with regard to preoperative or minimum 2-year follow-up PROs (Figure 5). There was no difference between the secondary ACI and secondary OCA groups with regard to the proportion of patients who were mostly or completely satisfied (81% vs 72%; $P$ = .73) (Figure 2). Clinical failure occurred in 12% (5 of 41) of the ACI cases and 10% (5 of 48) of the OCA cases ($P$ = .79), with 22% (10 of 46) and 20% (12 of 59) having >5-year follow-up in the secondary ACI and OCA groups, respectively. Among ACI cases, failures included 4 revisions to OCA and 1 to TKA. Among OCA cases, failures included 3 revisions to TKA and 2 to UKA. Kaplan-Meier survival analysis demonstrated no difference between ACI and OCA status post-MST with regard to graft survivorship ($P$ = .406) (Figure 6). Cox proportional hazards regression was performed to delineate predictors of failure of ACI and OCA. Workers' compensation status was the only independent predictor of failure ($P$ = .03), although there was a trend toward significance

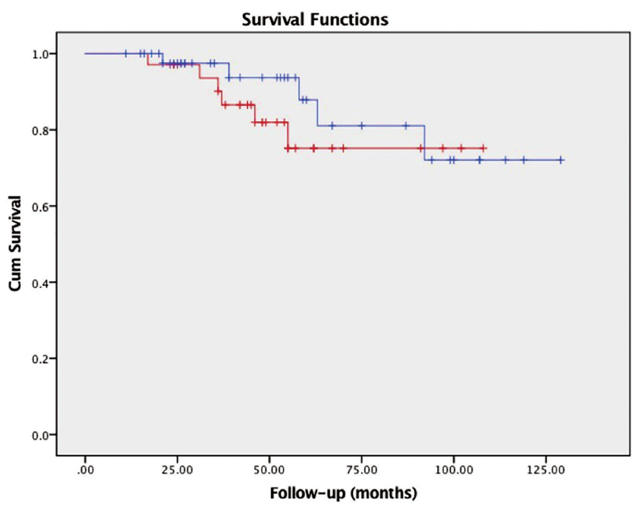


**Figure 6.** Kaplan-Meier survival curve demonstrates no difference in graft survivorship ($P$ = .406) between secondary autologous chondrocyte implantation (10 of 46 with >5-year follow-up) and secondary osteochondral allograft (12 of 59 with >5-year follow-up). Failure was defined by revision cartilage procedure, knee arthroplasty, or graft delamination/destruction on second look.

for increasing patient age ($P$ = .12). Surgical technique (OCA vs ACI; $P$ = .94), BMI ($P$ = .65), sex ($P$ = .56), and lesion area ($P$ = .27) were not predictors of failure. Reoperation rates for the ACI and OCA groups were 31% (13 of 42) and 25% (12 of 48) ($P$ = .53) (Figure 3).

## DISCUSSION

The goals of this study were (1) to compare outcomes of secondary ACI and OCA with those of primary ACI and OCA, respectively, and (2) to compare secondary ACI with secondary OCA to the femoral condyle to help define the roles of MST, ACI, and OCA in the algorithm for treating chondral lesions in the knee. We postulated that secondary ACI would render inferior functional outcomes and an increased clinical failure rate as compared with primary ACI, while secondary OCA would render equivalent outcomes to primary OCA and superior outcomes to secondary ACI. This study revealed the following: (1) ACI and OCA performed favorably after a failed MST, resulting in significant postoperative improvements in all evaluated PROs, with postoperative scores, subjective satisfaction rates, reoperation rates, and clinical failure rates that were comparable with primary ACI and OCA. (2) When age-, sex-, and BMI-matched cohorts of patients undergoing secondary ACI and OCA to the femoral condyle were evaluated, groups performed comparably with regard to PROs, subjective satisfaction, reoperation, and clinical failure.

ACI has been broadly demonstrated to be an effective treatment for full-thickness chondral defects of the knee, with authors consistently reporting good to excellent outcomes in >80% of patients. However, because of technical, patient, and lesion-specific factors, it remains difficult to determine the optimal place for ACI in the algorithm for treating chondral defects of the knee joint. Traditionally, ACI has been considered a second-line treatment (after failed debridement and/or MST) because of its expense and the multiple-stage nature of the procedure. However, some authors have suggested that ACI should be used more aggressively as a first-line treatment, as prior debridement and MST have been shown to compromise outcomes of ACI.[14,17]

Multiple studies in the literature have suggested inferior outcomes of secondary ACI as compared with primary ACI. Minas and colleagues[11] performed a large-scale series (N = 321) comparing clinical failure rates between patients who had undergone primary ACI and secondary ACI (with failure defined as persistent symptoms in the setting of magnetic resonance imaging [MRI] evidence of graft delamination, surgical removal of 25% of graft area, repeat cartilage procedure, or prosthetic replacement). The authors reported a dramatically higher rate of clinical failure in the MST cohort as compared with those treated with primary ACI (26% vs 8%). The authors suggested that prior marrow stimulation may result in unfavorable thickening of the subchondral bone and promote formation of an intralesional osteophyte, both of which compromise graft incorporation. Nevertheless, the authors noted that in a small cohort, they performed careful lesion preparation with a microbur to thin the thickened subchondral bone, and this technique seemed to result in a trend toward reduced failure rate. In other prior studies, MST was shown to cause inferior morphology of subchondral bone in addition to sclerosis and subchondral cysts.[15] Increased bone marrow edema was also shown to be a predictor of graft failure after ACI, further illustrating the importance of the subchondral bone.[10] To decrease the risk of ACI failure after an MST, intralesional osteophytes can be removed intraoperatively. However, a natural history study of these intralesional osteophytes by Demange et al[3] showed that while they often regrow, they are smaller when they do return. Pestka and colleagues[13] also reported a dramatically higher rate of clinical failure in patients with prior marrow stimulation (25% vs 3.6%) in a matched-pair series of 56 patients (28 undergoing primary ACI, 28 with a history of marrow stimulation). Finally, despite the lack of a control group undergoing primary ACI, Zaslav and fellow contributors[19] to the STAR clinical trial (Study of the Treatment of Articular Repair) reported a high rate of clinical failure in cases of ACI with a history of debridement (26%) and marrow stimulation (25%).

The literature comparing primary OCA with OCA status after MST is more limited, but what exists seems to suggest that results are unaffected by previous surgery. Gracitelli and colleagues[6] published the only series in the literature comparing the results of primary OCA with secondary OCA and reported comparable clinical outcomes, clinical failure rates, and patient satisfaction between groups.

The results of our study were consistent with those reported by Gracitelli and colleagues,[6] suggesting that there is no difference in results of primary OCA and secondary OCA. However, our results were inconsistent with those suggesting that prior MST increases the risk of failure for ACI, as primary ACI cases and ACI status post-MST cases demonstrated comparable PROs, subjective satisfaction, reoperation rates, and failure rates. The only factors that seemed to be predictive of failure were workers' compensation status and a trend toward significance with regard to advancing patient age.

We postulate that the most likely reason for the difference between our results and the available literature is patient selection. The overall failure rate in this study among patients in the entire ACI cohort (including primary and secondary ACI) was 10% (18 of 178). This compared favorably with failure rates reported by Minas et al[11] and Pestka et al[13] (14% each). This difference may be explained by the fact that patients in our series were significantly younger than those in the series by Minas et al and Pestka et al (mean age, 30.4 vs 35.1 and 33.9 years, respectively). Multiple studies have demonstrated detrimental effects of advanced patient age on the outcomes of ACI.[12,15] Additionally, in the series presented by Minas and colleagues, the prior MST group had larger lesions (520 $mm^2$ vs 460 $mm^2$) and a higher proportion of workers' compensation cases (22% vs 13%) than the primary ACI group, although not statistically significant.

After an MST fails, surgical treatment options are quite limited. OCA has demonstrated reliable outcomes in this setting and allows surgeons to avoid concerns regarding the integrity of the subchondral bony architecture. However, some surgeons are unable to perform OCA because of limited graft availability or cultural restrictions on the use of allograft tissue. Given the results of this study, surgeons can feel confident that, even after a failed MST, ACI can render reasonable PROs, with high rates of subjective satisfaction and low rates of clinical failure. Based on data suggesting poorer results of microfracture in lesions $>2$ $cm^2$, traditional algorithms favor ACI and OCA as first-line treatment for larger lesions, particularly in high-demand individuals.[2,11] While we would continue to advocate first-line treatment with ACI and OCA for large lesions, on the basis of this study, we would not recommend lowering the threshold for using these techniques in smaller lesions. For patients who have a failed prior MST, we recommend obtaining MRI to evaluate for the presence of an intralesional osteophyte or subchondral cystic change. If those anatomic changes are encountered, it is likely wise to favor OCA; however, in their absence, the surgeon may proceed with one's preferred technique. To optimize results of ACI, we recommend careful patient selection. ACI should be used cautiously in workers' compensation cases, patients aged $>30$ years, and those with BMI $>30$ $kg/m^2$, as all 3 have been associated with poorer outcomes.[5]

The most significant limitation of this study is its retrospective and nonrandomized design. Given the study's retrospective nature, there is the potential for selection bias in that patients with preoperative imaging suggestive of subchondral bony abnormality after an MST may have been more likely to be indicated for OCA than ACI. Preoperative MRI scans were not available for review in most cases to verify this bias. This patient cohort is also very heterogeneous with regard to lesion size and location, etiology, prior procedures, and concomitant procedures performed, making it difficult to ascertain the primary contributor to clinical failures. In addition, there were significant differences between the primary and secondary OCA groups in terms of meniscal allograft transplantation (MAT), illustrating the heterogeneity of the patients included. Finally, there was a variety of follow-up durations in the data, potentially introducing a selection bias in the noted number of failures. Additionally, many patients had additional procedures, which may have confounded the results. The strengths of this study derive from the large cartilage restoration cohort (n = 359 patients) treated by an experienced single surgeon with consistent indications, surgical technique, and rehabilitation.

## CONCLUSION

ACI and OCA are both viable treatment options for chondral defects of the knee, even in the setting of a failed MST. ACI in the setting of a failed MST renders functional outcomes, subjective satisfaction, reoperation rate, and failure rate comparable with primary ACI and with OCA.

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