Clinically Meaningful Improvement After Treatment of Cartilage Defects of the Knee With Osteochondral Grafts

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Background: Mosaicplasty and fresh osteochondral allograft transplantation (OCA) are popular cartilage restoration techniques that involve the single-stage implantation of viable, mature hyaline cartilage–bone dowels into chondral lesions of the knee. Recently, there has been greater focus on what represents a clinically relevant change in outcomes reporting, and commonly applied metrics for measuring clinical significance include the minimal clinically important difference (MCID) and substantial clinical benefit (SCB).

Purpose: To define the MCID and SCB after mosaicplasty or OCA for the International Knee Documentation Committee (IKDC) subjective form and Knee Outcome Survey–Activities of Daily Living (KOS-ADL) and to determine patient factors that are predictive of achieving the MCID and SCB after mosaicplasty or OCA.

Study Design: Cohort study (diagnosis); Level of evidence, 3.

Methods: An institutional cartilage registry was reviewed to identify patients who underwent mosaicplasty or OCA. The decision to perform either mosaicplasty or OCA was generally based on chondral defect size. The IKDC and KOS-ADL were administered preoperatively and at a minimum of 2 years postoperatively. Patient responses to the outcome measures were aggregated, and the MCID and SCB of these outcome scores were calculated with anchor-based methods. Multivariate analysis adjusted for age and sex was performed to identify patient factors predictive of achieving the MCID and SCB.

Results: Of the 372 eligible patients, 151 (41%) were lost to follow-up, 46 (12%) had incomplete preoperative outcome scores and 2 were treated with OCA of the tibia and therefore excluded. In total, 173 knees were analyzed (n = 173 patients; mean age, 33.0 years; 37% female). Seventy-five (43%) and 98 (57%) knees were treated with mosaicplasty and OCA, respectively. The mean ± SD MCIDs for the IKDC and KOS-ADL were 17 ± 3.9 and 10 ± 3.7, respectively. The SCBs for the IKDC and KOS-ADL were 30 ± 6.9 and 17 ± 3.9, respectively. Univariate analysis demonstrated no association between procedure (mosaicplasty or OCA) and likelihood of achieving the MCID or SCB. In the multivariate analysis, lower preoperative IKDC and KOS-ADL scores, higher preoperative Marx Activity Rating Scale scores, lower preoperative 36-Item Short Form Health Survey pain scores, and a history of ≤1 prior ipsilateral knee surgical procedure were predictive of achieving the MCID and/or SCB.

Conclusion: These values can be used to define a clinically meaningful improvement for future outcome studies. For surgeons considering mosaicplasty or OCA for their patients, these results can help guide clinical decision making and manage patient expectations before surgery.

Keywords: mosaicplasty; osteochondral autograft transfer; osteochondral allograft transplantation; clinical outcomes; minimal clinically important difference; substantial clinical benefit

Mosaicplasty (osteochondral autograft transfer) and fresh osteochondral allograft transplantation (OCA) are cartilage restoration techniques that involve the single-stage transfer of viable, mature hyaline cartilage. These procedures demonstrated 5- and 10-year survival rates >80% and high rates of patient satisfaction.[12,18,26] Given the ability of these structural osteochondral grafts to bear loads in the early postoperative period, treatment with mosaicplasty and OCA allows for a faster rehabilitation as compared with cell-based cartilage repair strategies, making these techniques increasingly popular among patients.

There is interest within surgical outcomes research in defining what constitutes clinically meaningful improvement after an operative intervention. As with much of the cartilage repair literature, studies reporting clinical outcomes after mosaicplasty and OCA traditionally defined

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success as statistically significant improvements in patient-reported outcome measures (PROMs) or by means of graft survivorship, with failure typically defined by evidence of graft collapse, need for revision procedure, or conversion to arthroplasty.[13,18,26,41-43] However, while statistical significance indicates that a difference is not likely the result of chance, whether the patient perceives this difference clinically is unknown. Furthermore, patients treated with cartilage repair generally consist of a younger active population, and those who are unsatisfied often decide to cope with pain and continue nonoperative treatment for numerous years before considering arthroplasty. For these reasons, better definitions of clinically meaningful improvement after cartilage restoration surgery are clearly desirable. Commonly used metrics for gauging clinical significance within outcomes reporting include the minimal clinically important difference (MCID) and substantial clinical benefit (SCB). The MCID is defined as the smallest difference in score from the domain of interest that patients perceive as being beneficial, while the SCB is the clinical value that the patient deems to be considerable improvement in health status.[14,23]

In 2010, Greco et al[16] calculated MCIDs for several PROMs with a group of patients treated surgically for articular cartilage defects of the knee. However, these patients received a variety of cartilage procedures, including debridement, shaving, drilling, autologous chondrocyte implantation (ACI), abrasion arthroplasty, microfracture, and cell therapy, and none were treated with mosaicplasty or OCA. Because osteochondral grafting procedures can have vastly different sequelae and rehabilitation timelines as compared with other cartilage repair techniques, the use of psychometric measures specific to mosaicplasty and OCA is essential for evaluating their surgical outcomes, particularly because of the increasing popularity of these procedures.[30] Therefore, the purposes of this study were (1) to define the MCID and SCB after mosaicplasty and OCA for the International Knee Documentation Committee (IKDC) subjective form and the Knee Outcome Survey–Activities of Daily Living (KOS-ADL) with an anchor-based method[23] and (2) to determine patient factors that are predictive of achieving the MCID and SCB after treatment with mosaicplasty and OCA. The hypothesis of this study was that lower preoperative knee outcome scores, higher preoperative activity levels, and fewer prior ipsilateral knee surgical procedures would be predictive of achieving the MCID and SCB after treatment with mosaicplasty and OCA.

METHODS

Study Design

A longitudinally maintained institutional registry dedicated to the tracking of patient outcomes after articular cartilage restoration procedures was retrospectively queried for patients who underwent mosaicplasty and OCA from 1999 to 2015. An institutional review board approved the institutional registry, and all the patients signed an informed consent form before participation.

For this study, inclusion criteria included (1) symptomatic focal cartilage lesions in the knee (up to 2 affected areas) that were classified as Outerbridge grade IV at the time of osteochondral grafting and did not involve substantial bone loss requiring shell allografts or additional bone grafting, (2) treatment with mosaicplasty or fresh OCA, and (3) a minimum of 2 years of outcomes follow-up. Exclusion criteria for these cartilage procedures were advanced osteoarthritis, simultaneous multiligamentous reconstruction, inflammatory arthritis or autoimmune conditions, and inability to comply with the postoperative rehabilitation protocol. Specific exclusion criteria for this study included incomplete pre- or postoperative data and treatment of tibial chondral lesions with osteochondral grafts.

Study Population Selection and Data Collected

Of the 1949 registry surgical procedures screened, 575 (30%) mosaicplasties and OCAs were performed. Only 372 of these were eligible for the minimum 2 years of follow-up (surgical date before February 9, 2015). Of these, 151 patients (41%) were lost to a minimum of 2 years of outcomes follow-up, leaving 221 patients who met the inclusion criteria. Forty-six patients (12%) did not have preoperative outcome scores and were excluded. Of the remaining knees, 2 were treated with OCA of the tibia and therefore excluded. As a result, the final study population consisted of 173 knees (173 patients).

Demographic, pre-, intra-, and postoperative data were collected for these patients. Demographic data included age, sex, and body mass index. Preoperative data included the number and type of previous ipsilateral knee surgical procedures and baseline PROMs. Standing lower limb alignment was assessed and recorded during the preoperative office visit. The use of preoperative long-leg radiographs to assess lower limb alignment was dependent on the surgeon's practice; for the majority of patients,

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long-leg radiographs were obtained only if gross malalignment was detected and osteotomy was being considered. Intraoperative data included laterality; examination under anesthesia (range of motion, ligamentous stability); location, size, and depth of the chondral defects; status of the articular surfaces in other compartments; meniscal status; and concomitant procedures performed. Postoperative data included postoperative rehabilitation protocol and PROMs at a minimum of 2 years after surgery.

Indications and Surgical Techniques for Mosaicplasty and OCA

Mosaicplasty or OCA was selected as the treatment option for these patients based on clinical judgment of defect complexity, location, and size, as well as failure of previous surgical or nonsurgical treatments. The decision to perform either mosaicplasty or OCA was based on chondral defect size; generally, mosaicplasty was performed for defects <2 cm^2 in total area and OCA for defects ≥ 2 cm^2. Prior failure of other cartilage restoration procedures (eg, microfracture) was not a contraindication for these procedures. ACI was rarely performed at our institution, owing to its 2-stage process and slower rehabilitation as compared with osteochondral grafting, and matrix-induced ACI (MACI) had not yet been approved by the Food and Drug Administration during the study period.

All surgical procedures were performed by 4 fellowship-trained orthopaedic surgeons (T.L.W, R.F.W, S.A.R, R.J.W.) at a single institution with extensive experience in cartilage repair procedures. After an examination under anesthesia, patients were treated with an initial diagnostic arthroscopy of the joint for assessment of the chondral lesion as well as the other articular surfaces, menisci, and ligaments. Any meniscal tears were addressed with partial meniscectomy or repair. A parapatellar arthrotomy was made either medially or laterally, depending on which location allowed for the best visualization of the lesion. The defect was then debrided to stable cartilage margins. Mosaicplasty was performed according to the method described by Hangody et al.[19] Donor osteochondral plugs were harvested by hand with commercially available instruments (Arthrex). All plugs were harvested from the intercondylar notch or superolateral margin of the trochlea. Plug diameters ranged from 6 to 10 mm, and the typical plug depth was 8 to 10 mm. Osteochondral plugs were placed flush with the surrounding articular cartilage, thus reconstituting the normal condylar architecture (Figure 1A). The mean ± SD number of plugs transferred was 2.2 ± 1.1. When multiple plugs were used, each successive plug was completely inserted before the core of bone from the next donor site was removed.

Fresh OCA was performed according to the dowel technique described by Williams et al.[46] Fresh cold-stored osteochondral allografts were obtained from commercially available sources. Donor tissue was screened and processed according to standards of the American Association of Tissue Banks.[29] Preoperatively, donor and recipient were matched on the basis of size with standard anteroposterior radiographs. Grafts were transplanted between 16 and 30 days after harvest, depending on serologic testing and patient availability. Chondral lesions were sized and reamed to a bed of normal bone. A similarly sized dowel was then harvested from the corresponding region of the osteochondral allograft. Lesion depth was carefully measured at 3 to 4 points around the lesion, marked, and matched on the donor tissue. Grafts were then gently impacted into place for press-fit fixation (Figure 1B). The mean number of dowels transplanted was 1.5 ± 0.7.

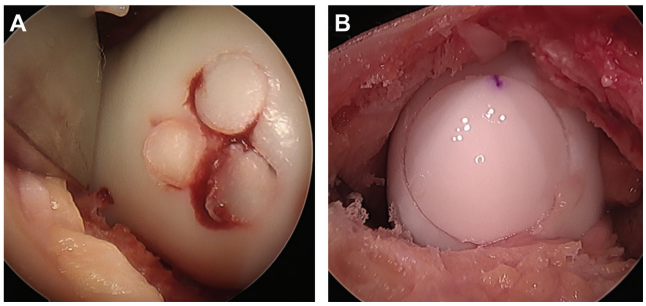

Figure 1. (A) Mosaicplasty of a femoral condyle with 3 osteochondral plugs and (B) osteochondral allograft transplantation of a femoral condyle with a single dowel.

Postoperatively, patients remained touchdown or nonweightbearing for a minimum of 1 to 2 weeks. Immediate full range of motion was permitted and encouraged with the use of a continuous passive motion device. Brace wear was discontinued at 2 to 6 weeks, based on restoration of quadriceps strength and function. A supervised physical therapy program was undertaken postoperatively in all cases. The duration of the postoperative physical therapy program depended on the restoration of normal gait, return of quadriceps function, and performance of sport-specific skills. Return to athletics was initiated on an individual patient basis, typically starting with a running program at 6 months. Higher-level activities were then progressed depending on return of lower extremity strength, coordination, balance, and proprioception.

Assessment of Outcomes

For patients included in the registry, outcomes were typically collected preoperatively and at 1, 2, 3, 4, 5, and 10 years postoperatively. Routine office follow-up was not generally expected from patients past 1 year postoperatively. Therefore, patients were contacted by email and phone for collection of postoperative outcomes. General health outcomes for each patient were assessed with the 36-Item Short Form Health Survey (SF-36; v 1.0),[31] which has the ability to evaluate 8 domains of general well-being. Only the pain and physical functioning subscales were evaluated in this study. Knee function was assessed with the IKDC,[21] KOS-ADL,[22] and subjective components of the Cincinnati Knee Rating System.[1] The IKDC score is a reliable and valid knee-specific measure of symptoms and function and was shown to provide a good overall measure of knee-related disability among patients treated with

a cartilage restoration procedure.[17,21] Similarly, the KOS-ADL and subjective components of the Cincinnati Knee Rating System were shown to have high reliability, validity, and responsiveness among athletic patients with various knee conditions.[27] Patient activity level was assessed with the Marx Activity Rating Scale.[28] An independent observer performed all pre- and postoperative data collection for these PROMs.

The MCID and SCB for the IKDC and KOS-ADL were calculated with an anchor-based method, in which a separate question "anchors" the change in outcome scores from baseline to minimum 2-year follow-up.[23] The anchor-based MCID is obtained by subtracting the mean change in outcome score of those reporting "no change" from the mean change of outcome score of those reporting "minimal improvement." Similarly, the anchor-based SCB is obtained by subtracting the mean change in outcome score of those reporting "no change" from the mean change of outcome score of those reporting "substantial improvement." Responses to PROMs from patients treated with mosaicplasty and OCA were analyzed as a single cohort. Physical function anchor questions were selected because domain-specific transition questions demonstrated higher construct validity as anchors for determining clinically important differences for health measures.[44]

For the anchor question of the IKDC, the MCID and SCB were defined with the patient perception component of the Cincinnati Knee Rating System regarding overall condition of the knee. This is a single item that asks patients to "rate the overall condition of your knee at the present time" using a numeric rating scale (1-10), with 2 indicating "poor—I have significant limitations that affect activities of daily living"; 4, "fair—I have moderate limitations that affect activities of daily living, no sports possible"; 6, "good—I have some limitations with sports but I can participate; I compensate"; and 10, "normal/excellent—I am able to do whatever I wish (any sport) with no problems."[1] There were 82 (47%) complete paired responses between the IKDC and overall condition scores. Pre- to postoperative changes in the overall condition scores were grouped so that differences of -2 to 2 points indicated "no change"; 3 to 4 points, "minimal improvement"; and $\geq$5 points, "substantial improvement."

For the anchor question of the KOS-ADL, the MCID and SCB were defined with the current function item of the IKDC. This single item is based on a numeric scale (0-10) that asks, "How would you rate the current function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?"[21] This item was used as the anchor question for the KOS-ADL rather than the patient perception component of the Cincinnati Knee Rating System for overall condition of the knee, given the higher percentage (n = 141, 82%) of complete paired responses between the KOS-ADL and the current function item of the IKDC. Pre- to postoperative changes in IKDC function scores were grouped so that differences of -1 to 1 point indicated "no change"; 2 to 4 points, "minimal improvement"; and $\geq$5 points, "substantial improvement."

Statistical Analysis

Comparisons between treatment groups were performed with the independent *t* test for continuous characteristics and chi-square or Fisher exact tests for discrete variables. Comparisons between pre- and postoperative outcome scores were performed with the paired *t* test. Preoperative IKDC and KOS-ADL score thresholds for the MCID and SCB were determined with receiver operating characteristic (ROC) curve analysis based on these preoperative scores, with the covariates of age and sex as the predictors and achievement of the MCID or SCB as the outcome. Age and sex were included in the logistic model to adjust for these demographic variables as potential confounders. The Youden index was used to determine the optimal point where sensitivity and specificity are maximized so that the ROC analysis yields the preoperative outcome score threshold at which patients are more or less likely to achieve the MCID or SCB. Predictive models are considered acceptable if the area under the curve (AUC) is $\geq$0.70 and excellent if $\geq$0.80.[4] Univariate logistic regression of patient-related factors, including demographic and clinical characteristics, was performed to evaluate the association between the single predictor of interest and achievement of the MCID or SCB. Clinical characteristics found to be significant at the .05 level in the univariate analysis were considered for inclusion in a multivariate logistic regression model. The final multivariate logistic model included clinical characteristics that were significant at the .05 level after adjusting for age and sex. All analyses were conducted with SAS (v 0.4; SAS Inc).

RESULTS

Patient Demographics and Clinical Characteristics

Of the 173 patients included in the study, the mean age was 33.0 $\pm$ 13.2 years, and 37% were female (Table 1). Seventy-five (43%) and 98 (57%) knees were treated with mosaicplasty and OCA, respectively. Mean age, number of prior ipsilateral knee surgical procedures, lesion location and area, and number of plugs implanted were significantly different between treatment groups. On average, patients undergoing mosaicplasty were younger, had fewer prior ipsilateral knee surgical procedures, had lower percentages of lateral femoral condylar and trochlear lesions and a higher percentage of patellar lesions, had a smaller total chondral defect area, and were treated with more plugs (Table 1).

Outcome Scores

The mean preoperative IKDC and KOS-ADL scores were 45.8 $\pm$ 14.7 and 63.8 $\pm$ 16.5, respectively, and the minimum 2-year postoperative scores were 69.1 $\pm$ 20.1 and 81.8 $\pm$ 14.6. Statistically significant improvements were noted in all outcome scores, with the exception of the

TABLE 1
Patient and Surgery Characteristics[a]

	All Knees (n = 173)	Mosaicplasty (n = 75)	OCA (n = 98)	*P* Value[b]
Patient characteristics				
Age, y	33.0 ± 13.2	29.8 ± 13.3	35.4 ± 12.5	<.01
Age <40 y	117 (68)	57 (76)	60 (61)	.05
Female sex	64 (37)	32 (43%)	32 (34)	.20
Body mass index, kg/m^2	25.8 ± 4.5	25.2 ± 4.6	26.2 ± 4.4	.17
No. of prior ipsilateral knee procedures	1.3 ± 1.5	0.7 ± 1.1	1.7 ± 1.6	<.01
Outcomes follow-up, y	2.7 ± 1.2	2.6 ± 1.3	2.7 ± 1.1	.46
Lesion characteristics				
Lesion location				
Medial femoral condyle	79 (46)	31 (41)	48 (45)	.36
Lateral femoral condyle	59 (34)	18 (24)	41 (42)	.02
Trochlea	28 (16)	6 (8)	22 (22)	.01
Patella	30 (17)	20 (27)	10 (10)	<.01
Total chondral defect area, cm^2	4.3 ± 2.6	2.3 ± 1.5	5.8 ± 2.3	<.01
No. of plugs used	1.7 ± 0.8	2.2 ± 1.1	1.5 ± 0.7	<.01
No. of concomitant procedures				
ACL reconstruction	2 (1)	1 (1)	1 (1)	≥.99
Meniscal allograft transplantation	7 (4)	2 (3)	5 (5)	.70
Realignment osteotomy	17 (10)	9 (12)	8 (8)	.45

[a]Data are reported as n (%) or mean ± SD. ACL, anterior cruciate ligament; OCA, osteochondral allograft transplantation.
[b]Comparison between mosaicplasty and OCA groups.

TABLE 2
Pre- and Postoperative Outcome Scores at Minimum 2-Year Follow-up[a]

Measure	Preoperative	Postoperative	*P* Value
SF-36			
Pain	53.2 ± 22.6	74.5 ± 21.2	<.01
Physical functioning	56.5 ± 23.1	81.0 ± 20.1	<.01
IKDC subjective form	45.8 ± 14.7	69.1 ± 20.1	<.01
KOS-ADL	63.8 ± 16.5	81.8 ± 14.6	<.01
Marx Activity Rating Scale	6.1 ± 6.4	5.1 ± 5.4	<.01
Cincinnati Knee Rating System			
Symptoms	4.8 ± 2.1	7.1 ± 2.6	<.01
Sports function	67.5 ± 28.3	76.5 ± 21.6	.02
Patient perception (overall condition)	4.3 ± 1.8	7.1 ± 2.1	<.01

[a]Values represent mean ± SD points. IKDC, International Knee Documentation Committee; KOS-ADL, Knee Outcome Survey–Activities of Daily Living; SF-36, 36-Item Short Form Health Survey.

TABLE 3
Psychometric Properties of IKDC and KOS-ADL[a]

	IKDC Subjective Form	KOS-ADL
Mean score		
Preoperative	45.8	63.8
Postoperative, 2 y	69.1	81.8
Mean 2-y outcome change	23.4	17.9
MCID	17	10
Proportion achieving, %	52.6	63.6
Score threshold	34	79
Strength of threshold	0.71	0.70
SCB	30	17
Proportion achieving, %	30.6	45.7
Score threshold	46	70
Strength of threshold	0.70	0.80

[a]IKDC, International Knee Documentation Committee; KOS-ADL, Knee Outcome Survey–Activities of Daily Living; MCID, minimal clinically important difference; SCB, substantial clinical benefit.

Marx Activity Rating Scale, which showed a statistically significant decrease from 6.1 ± 6.4 to 5.1 ± 5.4 at minimum 2-year follow-up (Table 2).

Minimal Clinically Important Difference

The MCID values for the IKDC and KOS-ADL were 17 (95% CI, 9.2-24.6) and 10 (95% CI, 2.8-17.3), respectively. ROC analysis adjusted for age and sex demonstrated score thresholds (AUC) of 34 (0.71) and 79 (0.70) for the IKDC and KOS-ADL, respectively (Table 3). The likelihood for achieving the MCID declined above these thresholds (Figure 2).

Substantial Clinical Benefit

The SCB values for the IKDC and KOS-ADL were 30 (95% CI, 16.1-43.0) and 17 (95% CI, 9.1-24.2), respectively. ROC analysis adjusted for age and sex demonstrated score thresholds (AUC) of 46 (0.70) and 70 (0.80) for the IKDC and KOS-ADL, respectively (Table 3). The likelihood for achieving the SCB declined above these thresholds (Figure 2).

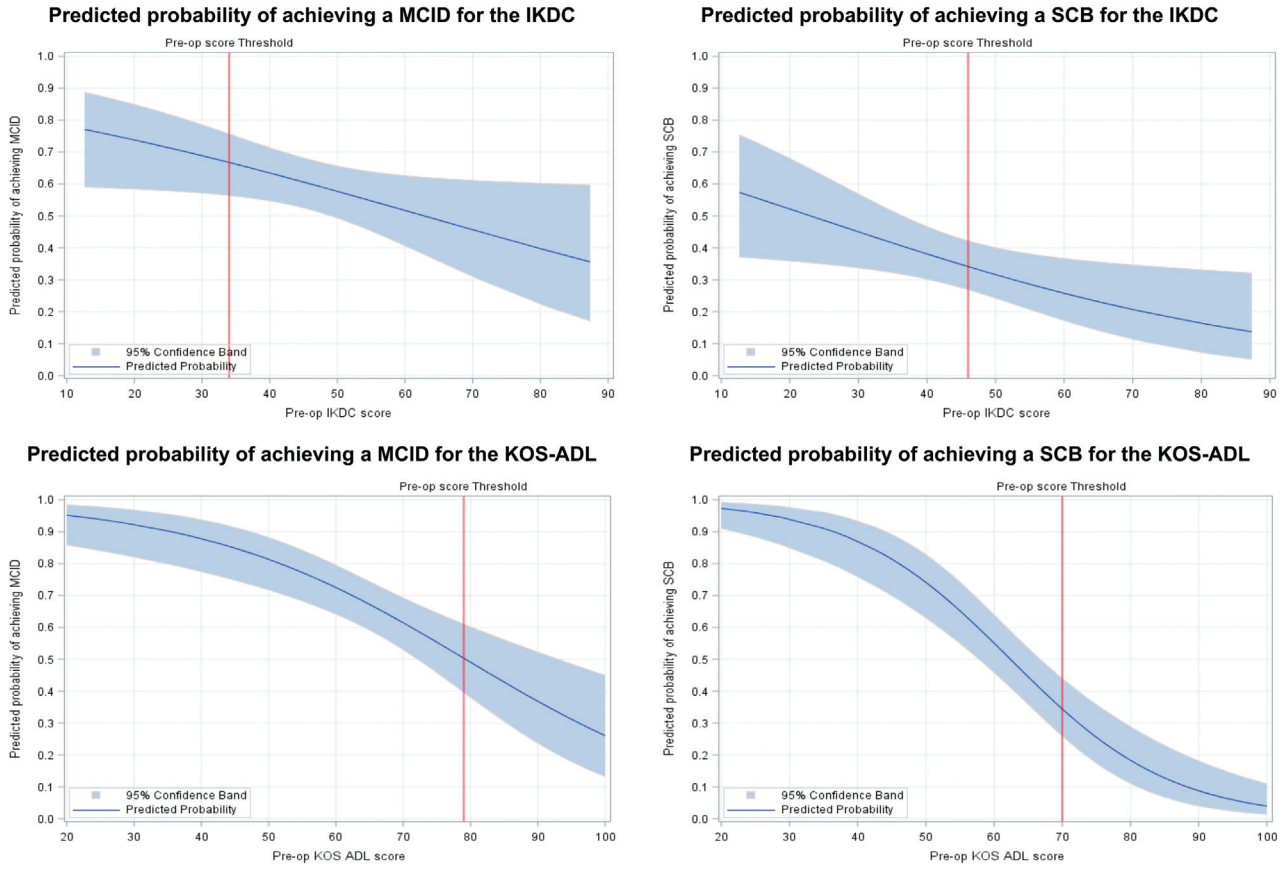

Figure 2. Preoperative score thresholds at which patients are more or less likely to achieve the minimal clinically important difference (MCID) and substantial clinical benefit (SCB) were calculated with receiver operating characteristic curve analysis adjusted for patient age and sex. For the International Knee Documentation Committee (IKDC) subjective form and the Knee Outcome Survey–Activities of Daily Living (KOS-ADL), the likelihood for achieving the MCID and SCB decreased as preoperative scores increased. The vertical lines demonstrate the preoperative scores thresholds that were most predictive of achieving the MCID and SCB (area under the curve $\geq$0.70). That is, patients with preoperative scores below these thresholds were more likely to achieve the MCID or SCB on the outcome measure.

Univariate and Multivariate Analysis

In the multivariate analysis adjusted for age and sex, significant predictors were identified for achieving the MCID on the IKDC and KOS-ADL (Table 4). For the IKDC, a lower preoperative IKDC score (odds ratio [OR], 1.04; 95% CI, 1.01-1.08) and higher preoperative Marx Activity Rating Scale score (OR, 1.11; 95% CI, 1.05-1.19) were predictive of achieving the MCID. For the KOS-ADL, $\leq$1 prior ipsilateral knee surgical procedure (OR, 3.16; 95% CI, 1.44-7.19), a lower preoperative KOS-ADL score (OR, 0.96; 95% CI, 0.93-0.99), and a lower preoperative SF-36 pain score (OR, 0.98; 95% CI, 0.96-1.00) were predictive of achieving the MCID. Preliminary univariate analysis also indicated that trochlear lesion location and preoperative IKDC score were associated with achieving the MCID for the IKDC and KOS-ADL, respectively (Table 5), but these factors dropped out in the multivariate analysis. In the univariate analysis, surgery type (mosaicplasty or OCA) was not associated with achieving the MCID and thus was not included in the multivariate analysis.

Similarly, in the multivariate analysis adjusted for age and sex, significant predictors were identified for achieving the SCB on the IKDC and KOS-ADL (Table 4). For the IKDC, a lower preoperative IKDC score (OR, 0.95; 95% CI, 0.92-0.97) and higher preoperative Marx Activity Rating Scale score (OR, 1.13; 95% CI, 1.06-1.21) were predictive of achieving the SCB. For the KOS-ADL, $\leq$1 prior ipsilateral knee surgical procedure (OR, 3.03; 95% CI, 1.29-7.35) and a lower preoperative KOS-ADL score (OR, 0.91; 95% CI, 0.88-0.94) were predictive of achieving the SCB. Preliminary univariate analysis also indicated that preoperative SF-36 pain and physical functioning scores and preoperative IKDC score were associated with achieving the SCB for the KOS-ADL (Table 6), but these factors dropped out in the multivariate analysis. In the univariate analysis, surgery type (mosaicplasty or OCA) was not significantly associated with achieving the SCB and thus was not included in the multivariate analysis.

TABLE 4
Multivariate Logistic Models for Achieving MCID and SCB[a]

	Odds Ratio (95% CI)	*P* Value
Achieving MCID on IKDC subjective form		
Age (≥40 y vs <40 y)	0.85 (0.40-1.83)	.68
Sex (female vs male)	1.25 (0.61-2.59)	.55
Preoperative IKDC subjective form	0.96 (0.93-0.99)[b]	<.01
Preoperative Marx Activity Rating Scale	1.11 (1.05-1.19)[b]	<.01
Achieving MCID on KOS-ADL		
Age (≥40 y vs <40 y)	0.92 (0.40-2.12)	.85
Sex (female vs male)	1.46 (0.67-3.24)	.34
No. of prior ipsilateral knee procedures (>1 vs ≤1)	0.32 (0.14-0.69)	<.01
Preoperative KOS-ADL	0.96 (0.93-0.99)[b]	.01
Preoperative SF-36 pain	0.98 (0.96-1.00)[b]	.04
Achieving SCB on IKDC subjective form		
Age (≥40 y vs <40 y)	0.50 (0.20-1.17)	.12
Sex (female vs male)	0.72 (0.33-1.55)	.41
Preoperative IKDC subjective form	0.95 (0.92-0.97)[b]	<.01
Preoperative Marx Activity Rating Scale	1.13 (1.06-1.21)[b]	<.01
Achieving SCB on KOS-ADL		
Age (≥40 y vs <40 y)	0.94 (0.41-2.12)	.88
Sex (female vs male)	1.43 (0.64-3.22)	.38
No. of prior ipsilateral knee procedures (>1 vs ≤1)	0.33 (0.14-0.78)	.01
Preoperative KOS-ADL	0.91 (0.88-0.94)[b]	<.01

[a]IKDC, International Knee Documentation Committee; KOS-ADL, Knee Outcome Survey–Activities of Daily Living; MCID, minimal clinically important difference; SCB, substantial clinical benefit; SF-36, 36-Item Short Form Health Survey.
[b]For each unit increase in score.

TABLE 5
Univariate Logistic Models for Achieving MCID[a]

	IKDC Subjective Form		KOS-ADL	
Variable	Odds Ratio (95% CI)[b]	*P* Value	Odds Ratio (95% CI)[b]	*P* Value
Age, ≥40 vs <40 y	0.86 (0.45-1.62)	.64	1.32 (0.67-2.59)	.42
Sex, female vs male	1.40 (0.75-2.60)	.29	1.43 (0.75-2.76)	.28
Body mass index, ≥30 vs <30 kg/m^2	0.89 (0.37-2.10)	.78	1.46 (0.57-3.75)	.43
Surgery, mosaicplasty vs OCA	1.54 (0.84-2.83)	.16	1.73 (0.92-3.28)	.09
Lesion location				
Medial femoral condyle vs other	0.90 (0.48-1.69)	.74	0.85 (0.44-1.62)	.61
Lateral femoral condyle vs other	0.87 (0.48-1.58)	.63	1.63 (0.87-3.05)	.13
Trochlea vs other	0.88 (0.39-1.98)	.76	0.43 (0.19-0.97)	.04
Patella vs other	0.88 (0.40-1.94)	.75	0.83 (0.37-1.86)	.65
No. of prior ipsilateral knee procedures, >1 vs ≤1	0.62 (0.31-1.21)	.16	0.46 (0.37-3.74)	.03
Meniscal tear, yes/no	0.86 (0.28-2.62)	.79	1.17 (0.37-3.74)	.79
Total chondral defect area, cm^2	1.00 (1.00-1.00)	.40	1.00 (1.00-1.00)	.58
Preoperative outcome scores				
SF-36 pain	0.99 (0.98-1.00)	.14	0.97 (0.95-0.99)	<.01
SF-36 physical functioning	1.00 (0.98-1.01)	.69	0.98 (0.97-1.00)	.01
IKDC subjective form	0.98 (0.95-1.00)	.04	0.97 (0.95-1.00)	.02
KOS-ADL	0.99 (0.97-1.01)	.16	0.95 (0.93-0.97)	<.01
Marx Activity Rating Scale	1.08 (1.03-1.13)	<.01	1.03 (0.98-1.08)	.33

[a]IKDC, International Knee Documentation Committee; KOS-ADL, Knee Outcome Survey–Activities of Daily Living; MCID, minimal clinically important difference; OCA, osteochondral allograft transplantation; SF-36, 36-Item Short Form Health Survey.
[b]For continuous variables, odds ratio is indicated for each unit increase.

TABLE 6
Univariate Logistic Models for Achieving SCB[a]

	IKDC		KOS-ADL	
Variable	Odds Ratio (95% CI)[b]	*P* Value	Odds Ratio (95% CI)[b]	*P* Value
Age, ≥40 vs <40 y	0.51 (0.24-1.06)	.07	1.29 (0.68-2.45)	.43
Sex, female vs male	0.83 (0.42-1.63)	.58	1.32 (0.71-2.45)	.38
Body mass index, ≥30 vs <30 kg/m^2	0.92 (0.36-2.38)	.87	1.81 (0.76-4.34)	.18
Surgery, mosaicplasty vs OCA	1.40 (0.73-2.67)	.32	1.73 (0.94-3.18)	.08
Lesion location				
Medial femoral condyle vs other	1.26 (0.64-2.47)	.50	1.01 (0.54-1.89)	.99
Lateral femoral condyle vs other	1.09 (0.57-2.09)	.79	1.20 (0.66-2.19)	.56
Trochlea vs other	0.72 (0.29-1.81)	.48	0.61 (0.26-1.42)	.25
Patella vs other	0.64 (0.26-1.60)	.34	0.76 (0.34-1.68)	.49
No. of prior ipsilateral knee procedures, >1 vs ≤1	0.51 (0.23-1.12)	.09	0.53 (0.26-1.08)	.08
Meniscal tear, yes/no	0.94 (0.27-3.23)	.92	0.88 (0.28-2.70)	.82
Total chondral defect area, cm^2	1.00 (1.00-1.00)	.33	1.00 (1.00-1.00)	.59
Preoperative outcome scores				
SF-36 pain	0.99 (0.98-1.01)	.21	0.96 (0.95-0.98)	<.01
SF-36 physical functioning	1.00 (0.99-1.02)	.77	0.97 (0.96-0.98)	<.01
IKDC	0.97 (0.95-1.00)	.02	0.95 (0.93-0.98)	<.01
KOS-ADL	0.99 (0.97-1.01)	.27	0.92 (0.89-0.95)	<.01
Marx Activity Rating Scale	1.10 (1.04-1.16)	<.01	0.99 (0.95-1.04)	.72

[a]IKDC, International Knee Documentation Committee; KOS-ADL, Knee Outcome Survey–Activities of Daily Living; OCA, osteochondral allograft transplantation; SCB, substantial clinical benefit; SF-36, 36-Item Short Form Health Survey.
[b]For continuous variables, odds ratio is indicated for each unit increase.

DISCUSSION

In recent years, mosaicplasty and OCA have been among the most commonly performed cartilage restoration procedures for articular cartilage defects because of their single-stage transfer of viable, mature hyaline cartilage–bone dowels, allowing for faster postoperative rehabilitation when compared with cell-based techniques.[30] For these osteochondral grafting procedures, we defined the MCID and SCB for the IKDC and KOS-ADL and found that higher preoperative outcome scores decreased the likelihood of achieving the MCID and SCB on each minimum 2-year postoperative outcome score. Additionally, several other predictive factors were identified through the multivariate analysis. Higher preoperative activity levels, as defined by the Marx Activity Rating Scale, were predictive of achieving the MCID and SCB on the IKDC; lower preoperative SF-36 pain scores, indicating less pain, were predictive of achieving the MCID on the KOS-ADL; and a history of ≤1 prior ipsilateral knee surgical procedure was predictive of achieving the MCID and SCB on the KOS-ADL.

Much of the literature reporting on outcomes after mosaicplasty and OCA traditionally defined clinical success as it relates to graft survivorship, with failure defined by evidence of graft collapse, need for revision procedure, or conversion to arthroplasty.[13,18,26,41-43] However, the patient population treated with cartilage repair is generally younger, and if unsatisfied, these patients often decide to cope with pain and continue nonoperative treatment for numerous years before eventually considering arthroplasty. As a result, better definitions of clinically meaningful improvement after cartilage restoration surgery are clearly desirable. Within orthopaedic surgery, there is an increased interest in defining a clinically meaningful patient outcome after an operative intervention. Although psychometric measures of a clinically significant change on knee-specific PROMs for anterior cruciate ligament (ACL) reconstruction,[34,35] meniscal injuries,[6] and knee osteoarthritis[40,47] were previously investigated, there is a paucity of information on what constitutes clinically important improvements after cartilage restoration procedures. Greco et al[16] administered PROMs to a group of patients with focal articular cartilage defects treated with surgery and calculated an MCID on the IKDC of 16.7 at 12 months. However, these patients received a variety of cartilage procedures, including debridement, shaving, drilling, ACI, abrasion arthroplasty, microfracture, and cell therapy; none were treated with mosaicplasty or OCA. In another study, Ebert et al[10] calculated 5-year MCID values of 31 to 40 on the Knee injury and Osteoarthritis Outcome Score among patients treated with MACI. Nevertheless, the progression of full weightbearing, running, performance of sport-specific movements, and return to athletics is significantly faster in the early postoperative period for osteochondral grafting as compared with ACI and MACI owing to the implantation of mature grafts, whereas time is needed for cell-based grafts to mature.[20,24] Therefore, the rates of clinically meaningful improvement likely differ between osteochondral grafting and cell-based techniques at early postoperative intervals. This necessitates the use of psychometric measures specific to mosaicplasty and OCA for the measurement of their 2-year surgical outcomes.

In this study, higher baseline IKDC and KOS-ADL scores decreased the likelihood of achieving the MCID and SCB on each outcome measure, suggesting that patients starting with high preoperative scores may have less opportunity for postoperative improvement that would meet the criteria for the MCID and SCB. Similar findings were reported for PROMs of postoperative improvement after shoulder arthroplasty,[45] total hip arthroplasty,[4] hip arthroscopy,[36] ACL reconstruction,[35] and total knee arthroplasty.[3] The preoperative score thresholds calculated in this study, which were all acceptably predictive (AUC $\geq$0.70), can provide clinicians with objective indicators to predict the possibility of meaningful improvement after mosaicplasty and OCA and are therefore useful for managing patient expectations before surgery.

Additionally, higher preoperative activity levels and lower preoperative pain scores were predictive of achieving the MCID and SCB in this study. These results fit the clinical picture of patients with higher baseline physical activity levels, stronger knee and core musculature, and less overall pain (or higher pain tolerances). These patients are typically able to rehabilitate vigorously, which allows them to maximize the trajectory of their recovery and ultimate success after surgery. Similar findings of a correlation between higher preoperative activity level and good outcomes after surgery were reported for ACI[48] and ACL reconstruction.[7,8] Moreover, a history of $\leq$1 prior ipsilateral knee surgical procedures was predictive of achieving the MCID and SCB in this study. This corresponds with results from the literature demonstrating that higher numbers of prior ipsilateral knee surgical procedures predict a higher risk of revision cartilage surgery or conversion to arthroplasty after OCA.[12,15,26,41,43] In contrast to ACI or MACI, mosaicplasty and OCA are not negatively influenced by any damage to the subchondral bone from prior cartilage repairs, because the subchondral bone is excised and substituted by the donor bone. Therefore, the correlation of a higher number of prior knee surgical procedures with failure to achieve the MCID and SCB may be related to prolonged knee dysfunction and duration of symptoms, the latter of which was not investigated in this study. A longer duration of symptoms was shown to be a negative predictor of good outcomes and return to sport after cartilage restoration.[5,9,25,32,33,37]

This study has several limitations worth noting. A major limitation is the potential bias associated with the incomplete pre- and postoperative outcome data, as 41% of patients were excluded for loss of follow-up and 12% were excluded for incomplete preoperative outcome scores. Some patients who did not follow-up may have had worse outcomes or undergone treatment with knee arthroplasty. Conversely, other patients who did not follow-up may have had excellent outcomes and were less motivated to complete the 2-year PROMs. Nevertheless, unlike distribution-based approaches, the anchor-based method does not rely on the statistical characteristics of the obtained samples and instead compares the change in outcome score with a concurrently collected external measure of change. Therefore, this follow-up loss is unlikely to affect the calculated MCID and SCB values. Additionally, only a subset of the patients analyzed in this study had complete paired responses between the knee-specific PROMs and their anchor questions (47% for IKDC and overall condition anchor; 82% for KOS-ADL and IKDC anchor). Despite this, the anchor-based method was still the optimal approach, given that the proportion of patients who do well after cartilage restoration procedures is highly variable and not well accepted. Moreover, the subset populations for each analysis were still sufficiently large to calculate MCID and SCB values with appropriate reliability and validity. Although using a separate prospective satisfaction anchor question would have been ideal, the anchor questions used in this study were determined to be the best options given the available data.

Second, because this study was a retrospective review of a longitudinally maintained institutional database, it was subject to selection bias and assessment bias. The patients were treated by surgeons at a single institution performing a high volume of mosaicplasty and OCA, which reduces the generalizability of these findings to other settings. Additionally, although this study used function-based anchors belonging to validated PROMs, each anchor item had not been individually validated. However, these anchors were generally concordant with the other metrics used in this study, thus attaining face validity.

Third, a limitation of determining the MCID and SCB for PROMs is that the degree of change in a measure is often associated with the baseline state and therefore influenced by any ceiling effects of the PROMs.[2] For the KOS-ADL, the higher baseline scores and a higher threshold value for the MCID as compared with the SCB indicate a ceiling effect for this measure in this patient population.

Fourth, mosaicplasty and OCA are different procedures with different indications, resulting in differences between groups in patient and surgical characteristics. These surgical procedures are not identical: mosaicplasty is done with autologous tissue and thus has donor-site morbidity, while an immune response may be invoked by allograft tissue transplantation. However, these procedures were analyzed as a single cohort to obtain an appropriate level of power needed for this study.

Finally, 14% of the study population received a concomitant procedure, which may have affected the final outcomes. Nevertheless, concomitant procedures are frequently performed with cartilage restoration procedures to treat the underlying cause of the chondral lesion (eg, instability, malalignment, meniscal deficiency). Other studies on mosaicplasty and OCA reported that up to 52% to 85% of patients received concomitant procedures in their series.[12,18,38] Additionally, several comparative studies suggested that ACL reconstruction and meniscal allograft transplantation do not negatively affect the patient-reported outcomes of OCA.[11,39,41]

CONCLUSION

For the treatment of cartilage defects of the knee with osteochondral grafts, higher preoperative IKDC and KOS-ADL scores decreased the likelihood of achieving

the MCID and SCB on each minimum 2-year postoperative outcome score. Additionally, higher preoperative activity levels, as defined by the Marx Activity Rating Scale, were predictive of achieving the MCID and SCB on the IKDC; lower preoperative SF-36 pain scores, indicating less pain, were predictive of achieving the MCID on the KOS-ADL; and a history of ≤ 1 prior ipsilateral knee surgical procedures was predictive of achieving the MCID and SCB on the KOS-ADL. The MCID and SCB values derived in this study are novel additions to the literature that may serve as references for defining a minimal clinically important change and SCB in subsequent studies utilizing patient-reported outcomes. For studies reporting the clinical outcomes of mosaicplasty and OCA, using a standardized definition of clinically meaningful improvement is essential for comparing outcomes between patient groups or other cartilage restoration procedures. Furthermore, for surgeons considering mosaicplasty or OCA for their patients, these results can help guide clinical decision making and manage patient expectations before surgery.

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