Fresh Osteochondral Allografts in the Knee: Comparison of Primary Transplantation Versus Transplantation After Failure of Previous Subchondral Marrow Stimulation

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Fresh Osteochondral Allografts in the Knee

Comparison of Primary Transplantation Versus Transplantation After Failure of Previous Subchondral Marrow Stimulation

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Background: In most treatment algorithms, osteochondral allograft (OCA) transplantation is regarded as an alternative salvage procedure when other, previous reparative treatments have failed.

Purpose: To compare the outcomes of a retrospective matched-pair cohort of (1) primary OCA transplantation and (2) OCA transplantation after failure of previous subchondral marrow stimulation.

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

Methods: An OCA database was used to identify 46 knees that had OCA transplantation performed as a primary treatment (group 1) and 46 knees that underwent OCA transplantation after failure of previous subchondral marrow stimulation (group 2). All patients had a minimum of 2 years' follow-up. Patients in each group were matched for age (±5 years), diagnosis (osteochondral lesion, degenerative chondral lesion, traumatic chondral injury), and graft size (small, <5 cm^2; medium, 5-10 cm^2; large, >10 cm^2). The groups had similar body mass indexes, sex distributions, and graft locations (femoral condyle, patella, and trochlea. The number and type of further surgeries after the OCA transplantation were assessed; failure was defined as any reoperation resulting in removal of the graft. Functional outcomes were evaluated by use of the modified Merle d'Aubigné-Postel (18-point) scale, International Knee Documentation Committee (IKDC) subjective knee evaluation form, Knee injury and Osteoarthritis Outcomes Score (KOOS), and the Knee Society function (KS-F) scale. Patient satisfaction, according to a 5-point scale from ''extremely satisfied'' to ''dissatisfied,'' was recorded at the latest follow-up.

Results: Eleven of 46 knees (24%) in group 1 had reoperations, compared with 20 of 46 knees (44%) in group 2 ($P = .04$). The OCA was classified as a failure in 5 knees (11%) in group 1 and 7 knees (15%) in group 2 ($P = .53$). At 10 years of follow-up, survivorship of the graft was 87.4% and 86% in groups 1 and 2, respectively. Both groups showed improvement in pain and function on all subjective scores from preoperatively to the latest follow-up (all $P < .001$). Results showed that 87% of patients in group 1 and 97% in group 2 were ''satisfied'' or ''extremely satisfied'' with the OCA transplantation.

Conclusion: Favorable results were shown in both groups with significant improvement of functional scores and excellent survivorship. Despite the higher reoperation rate in the previously treated group, previous subchondral marrow stimulation did not adversely affect the survivorship and functional outcome of OCA transplantation.

Keywords: osteochondral allograft transplantation; cartilage repair; matched cohort

Cartilage lesions are common injuries, described in 63% of patients who have an arthroscopy[7] and more than 50% of asymptomatic athletes.[11] The patella (37%) and the medial femoral condyle (35%) were found to be the most common lesion sites.[11] Cartilage injuries can be caused by osteochondritis dissecans (OCD), avascular necrosis (AVN), and repetitive or acute trauma. Frequently, OCD and AVN cause osteochondral defects and require multiple surgical interventions.[10,12] Isolated cartilage injuries can cause major clinical problems and functional impairment.[15] If left untreated, the cartilage injury may worsen over time and degenerate to osteoarthritis.[8]

The treatment of cartilage lesions remains a challenge in orthopaedic surgery. Nonsurgical treatment can relieve symptoms but cannot restore cartilage. Many surgical treatments available are based on cartilage repair, including autologous chondrocyte implantation (ACI), subchondral marrow stimulation (SMS), osteochondral autograft transplantation (OAT), and osteochondral allograft (OCA) transplantation. Patients with cartilage lesions tend to be young and very active, requiring multiple and variable

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interventions after a failed cartilage restoration technique, according to algorithms in the literature.[1,4,28]

The effect of a previous cartilage surgery on subsequent cartilage restoration procedures is controversial. Historically, SMS techniques such as microfracture, drilling, and abrasion arthroplasty have been considered a reasonable first-line treatment because SMS was believed not to hinder any further surgeries. More caution has been advised recently regarding successive interventions for cartilage repair. It was shown that ACI after previous treatment with SMS interventions failed at a rate 3 to 5 times higher than the failure rate of primary ACI.[22,25]

Fresh OCA transplantation is increasingly used and is suitable as a salvage procedure to treat large cartilage lesions, which are frequently found after successive failures of cartilage repair attempts.[3,20] Transplantation with OCA entails an equivalent-sized fragment of fresh allograft cartilage with supportive subchondral bone that is transplanted into the cartilage defect. Transplantation of OCA can restore the defect to an architecturally accurate and mature hyaline cartilage.[20]

The aim of the present study was to examine the influence of previous cartilage repairs on subsequent OCA transplantation. For this purpose, we designed a retrospective matched-pair cohort of (1) primary OCA transplantation compared with (2) OCA transplantation after failure of previous subchondral marrow stimulation.

MATERIALS AND METHODS

Our institutional review board–approved OCA database at Scripps Clinic was used to identify a consecutive series of 46 knees that had OCA transplantation, with a minimum follow-up of 2 years, performed as a primary treatment (group 1). These were matched to a nonconsecutive series of 46 knees that underwent OCA transplantation after failure of previous subchondral marrow stimulation (group 2). All OCA transplantations were performed between 1983 and 2011 by 2 surgeons, and all knees had a minimum of 2 years' follow-up. The indications for surgery were isolated osteochondral lesions with International Cartilage Repair Society (ICRS) grades 3 and 4, patients who had failed previous surgical and nonsurgical interventions, and/or patients who wished to avoid prosthetic arthroplasty. Our exclusion criteria were patients with less than 2 years of follow-up.

Patients were matched 1:1 by known predictors of functional outcome and allograft survivorship,[14,20] such as age (±5 years), diagnosis (osteochondral lesion [OCD/AVN], degenerative chondral lesion, traumatic chondral injury), and graft size (small, <5 cm^2; medium, 5-10 cm^2; large, >10 cm^2). The groups had similar body mass indexes, sex distributions, and graft locations (Table 1). This study included predominantly femoral condyle transplantation (91.3% in group 1 and 95.7% in group 2) and SMS (drilling or microfracture) as the previous procedure (all cases of group 2).

The number and type of further surgeries after the OCA transplantation were assessed. We defined failure of the OCA as any reoperation resulting in removal of the graft, such as allograft revision and any form of arthroplasty.

Available patients were examined in the clinic to measure current pain levels, joint function, and satisfaction with the procedure, or the patients were contacted by telephone if they were unable to return for clinical follow-up. Patients who underwent reoperation in other institutions had follow-up by telephone only. Clinical scores were obtained by mailed questionnaires. Pain and function were measured preoperatively and at final follow-up with the modified Merle d'Aubigné-Postel (18-point) scale, International Knee Documentation Committee (IKDC) subjective knee evaluation form,[17] Knee injury and Osteoarthritis Outcome Score (KOOS),[26] and Knee Society function (KS-F) scale.[16] The Merle d'Aubigné-Postel (18-point) scale was modified with the range of motion feature (ROM) values relevant to the knee rather than the hip. This scale includes physical examination characteristic and includes a maximum of 6 points each for pain, knee ROM, and knee function, for a total of 18 points.

Patient satisfaction was recorded at latest follow-up using a 5-point scale with the qualifiers "extremely satisfied," "satisfied," "somewhat satisfied," "somewhat dissatisfied," and "dissatisfied."

Surgical Technique

All surgeries were performed through a medial or lateral parapatellar arthrotomy. The size of the lesion was recorded. The nonviable tissue found was debrided and prepared down in a geometric format to a depth of 2 to 10 mm (Figure 1, A and B). For lesions smaller than 10 cm^2, a dowel technique was used (Figure 1). For lesions larger than 10 cm^2, a shell allograft technique was chosen, as described in our previous reports.[20,24] To decrease the immunogenicity of the graft, the immunogenic marrow elements from the osseous surface were washed out with pulsatile lavage. The graft was trimmed into a shape matching the lesion (Figure 1C), and trial fittings were

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TABLE 1
Patient Information and Clinical Assessment[a]

	Group 1 (Primary Treatment)	Group 2 (Failed Subchondral Marrow Stimulation)
Age, y, mean ± SD	27.5 ± 11.8	26.2 ± 10.4
Sex, male/female, n	28/18	28/18
Body mass index, kg/m^2, mean ± SD	25.0 ± 5.1	25.2 ± 5.0
Diagnosis, n (%)		
AVN/OCD	42 (91)	42 (91)
DCL	1 (2.2)	1 (2.2)
TCI	3 (6.5)	3 (6.5)
Graft location, n (%)		
Femoral condyle	42 (91)	44 (96)
Medial	28 (66)	27 (61)
Lateral	11 (26)	14 (31)
Medial/lateral	3 (7)	3 (7)
Patella	1 (2)	1 (2)
Trochlea	3 (6)	1 (2)
Allograft size, cm^2, mean ± SD	8.2 ± 3.6	8.0 ± 3.2
No. of allografts, n		
1	31	37
2	15	10
3	3	2

[a]AVN, avascular necrosis; DCL, degenerative chondral lesion; OCD, osteochondritis dissecans; TCI, traumatic chondral injury.

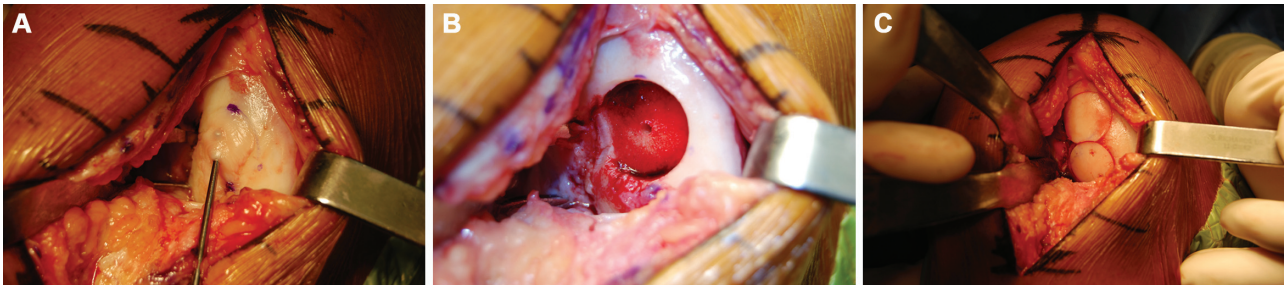

Figure 1. Dowel technique after a failed microfracture in the femoral condyle. (A) A medial arthrotomy is performed and the failed microfracture is identified. (B) The diameter of the defect is measured, and the lesion is prepared for 2 plugs. (C) The allografts are trimmed and inserted into the defect with the ''snowman'' technique.

performed until a well-positioned graft was achieved. The grafts were fixed either by press-fit fixation or with the use of bioabsorbable pins (Chondral Dart; Arthrex).

Postoperatively, patients with OCA transplantation in the femoral condyle were recommended full active ROM with no weightbearing for 8 to 12 weeks. With patellar and trochlear transplantation, patients were allowed weightbearing as tolerated with the knee locked in extension for 3 to 4 weeks. Generally, patients were allowed to participate in recreational and sports activities after 6 months.

Statistical Analysis

Means and frequencies were used to describe patient demographics (age, sex, body mass index, number of previous surgeries on operated knee, diagnosis), allograft details (size, number of grafts, location), and follow-up data (number and type of further surgeries, patient satisfaction). Survivorship of the OCA transplantation, with failure of the allograft used as the endpoint, was calculated by use of the Kaplan-Meier method. The two survivorship distributions were compared using the log rank test. Among patients whose grafts remained in situ at the latest follow-up, the Wilcoxon signed rank test was used to compare changes within each group from the preoperative state to the follow-up on the modified Merle d'Aubigné-Postel, IKDC, KOOS, and KS-F scales. Mann-Whitney U tests were used to compare mean scores between groups preoperatively and at the latest follow-up and to compare change from the preoperative state to the follow-up visit (difference scores). Statistical significance was set at $P < .05$. SPSS version 13.0 was used for all analyses (IBM Corp).

RESULTS

Eleven of 46 knees (24%) in group 1 had reoperations (ranging from 1 to 2 surgeries), compared with 20 of 46

TABLE 2
Frequency and Type of Reoperations After OCA Transplantation[a]

Reoperation	Group 1 (Primary Treatment)	Group 2 (Failed Subchondral Marrow Stimulation)
Arthroscopic debridement, diagnosis, or loose body removal	6	15
Meniscectomy	—	3
Meniscal repair	1	3
Extensor mechanism realignment	—	1
Lateral retinacular release	1	2
Osteotomy	—	1
Hardware removal	—	3
Reoperation defined as allograft failure		
Revision of allograft	2	3
Total knee arthroplasty	3	4

[a]Values are reported as number of knees. Some knees had >1 reoperation.

knees (44%) in group 2 (ranging from 1 to 4 surgeries) (Table 2). A significant difference in reoperation rate was found between groups ($P = .04$). The OCA transplantation was classified as a failure in 5 knees (11%) in group 1, of which 2 knees had the OCA revised and 3 were converted to total knee arthroplasty. In group 2, there were 7 knees (15%) that were considered failures, of which 3 knees had the OCA revised and 4 were converted to total knee arthroplasty. The failure rate was not statistically significant between groups ($P = .53$). At 10-year follow-up, similar survivorship of the allograft was found, with 87.4% in group 1 and 86% in group 2 (Figure 2). The 2 survivorship distributions were not statistically different ($P = .841$).

Patients whose grafts remained in situ had a mean (± SD) follow-up duration of 7.8 ± 5.1 years (41 knees in group 1) and 11.3 ± 6.6 years (39 knees in group 2) ($P = .01$). Both groups had improvement in pain and function from the preoperative point to the latest follow-up (all $P < .001$). No differences between groups were found preoperatively, at the latest follow-up, or in the change from preoperative state to follow-up (Table 3). Eighty-seven percent of patients in group 1 and 97% in group 2 were "satisfied" or "extremely satisfied" with the OCA transplantation.

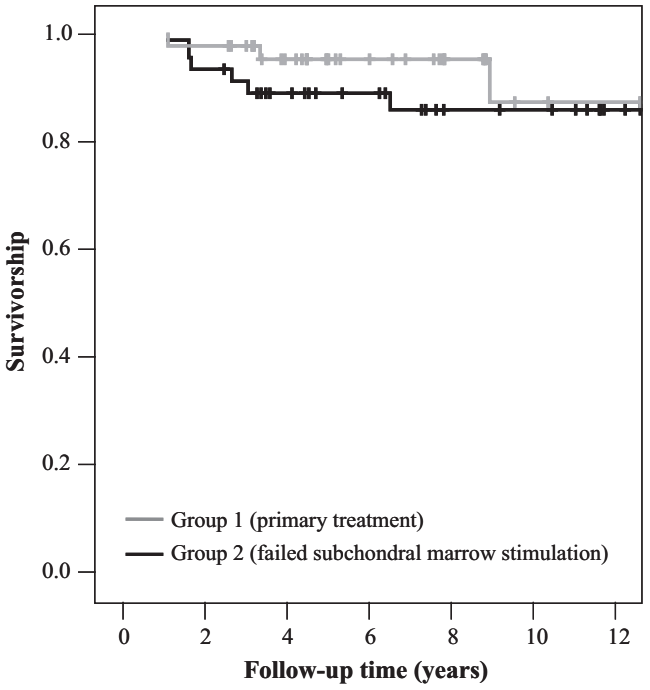

Figure 2. Kaplan-Meier survivorship with revision of the allograft or conversion to arthroplasty as the endpoint.

DISCUSSION

This study reported a survivorship of 87.4% in group 1 and 86% in group 2 at 10 years. Improvement in functional outcome scores was seen in both groups. An 87% good and excellent result was noted in both groups as assessed with the modified Merle d'Aubigné-Postel (18-point) scale. A statistically significant higher reoperation rate was found in the previously treated group ($P = .04$). To our knowledge, this is the first comparative study with a long follow-up time in OCA transplantation. The results found were similar to the results of our previously published cohorts of OCA transplantation[10,12,20,24] and other OCA transplantation studies.[6,14,19,21]

Other studies have shown good outcome when reporting OCA of the femoral condyle. LaPrade et al[19] reported 23 consecutive patients who had OCA transplantation of the femoral condyle with 3 years of follow-up. Eighty-seven percent of the patients had a prior procedure in the knee such as SMS, arthroscopy, loose body removal, and meniscectomy. Functional outcomes measured by IKDC improved significantly from a mean of 52 points to 68.5 points at the time of the final follow-up. McCulloch et al[21] reported 25 patients after OCA transplantation of the femoral condyle with average follow-up of 35 months. Twenty-four knees (96%) had previous procedures such as OCD fixation, debridement, microfracture, and ACI. Significant improvements in IKDC, KOOS, and the Short Form–12 were documented. Eighty-four percent of the patients reported to be satisfied with the treatment. Chu

TABLE 3
Pain and Function Measured Preoperatively and at Follow-up[a]

Measure	Group 1 (Primary Treatment)			Group 2 (Failed Subchondral Marrow Stimulation)			*P* Value[b]
	Preoperative	Follow-up	Difference	Preoperative	Follow-up	Difference	
Modified Merle d'Aubigné-Postel (18 point)	12.7	16.6	3.9	12.9	16.2	3.2	.46
% Excellent (18)	—	39		2.6	32		
% Good (15-17)	18	49		21	55		
% Fair (12-14)	58	13		50	8		
% Poor (<12)	25	—		26.3	5		
IKDC							
Pain	6.2	2.4	−4.2	5.4	2.6	−3.2	.09
Function	2.9	7.8	5.1	3.5	7.5	4.4	.34
Total	36.9	78.2	45.6	41.8	78.8	38.3	.29
KS-F	68.9	89.5	23.8	68.2	91.9	24.8	.86
KOOS subscale							
Symptoms	57.8	87.8	27.5	53.0	79.8	31.2	.81
Pain	65.6	89.9	31.2	64.3	82.1	10.0	.06
ADL	72.0	94.5	29.3	70.9	87.1	14.0	.11
Sport/Rec	37.5	72.7	40.6	30.6	70.7	43.3	.41
QOL	28.2	69.5	45.5	25.0	64.6	47.0	.92

[a]Values are reported as means. ADL, activities of daily living; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; KS-F, Knee Society function; QOL, quality of life; Sport/Rec, sport and recreation.
[b]*P* value for Mann-Whitney *U* test to compare difference scores between groups (change from preoperative state to latest follow-up) and chi-square test to compare postoperative score distributions between groups on the modified Merle d'Aubigné-Postel (18-point) scale.

et al[6] reported a series of 55 knees after OCA transplantation. The population was heterogeneous and had several diagnoses, such as OCD, AVN, traumatic chondral injury, and patellofemoral injuries. The authors showed that 55 (76%) of the knees were rated as good to excellent. When only unipolar femoral condyle transplants were analyzed, 84% were rated good to excellent. Levy et al[20] showed a cohort of 122 patients with femoral condyle lesions treated with OCA transplantation that included 40% of patients treated previously with SMS. The functional outcomes improved significantly, and the survivorship was 82% at 10 years and 74% at 15 years.

As shown above, all retrospective cohorts of OCA transplantation included patients previously treated with cartilage repair procedures or another type of surgery. No study was designed to analyze the influence of previous cartilage repair procedure on the final outcome of OCA transplantation. This study is the first comparative study that created homogeneous groups to assess the influence of SMS in the subsequent OCA transplantation.

In our study, both groups showed a high reoperation rate (24% in group 1 and 44% in group 2), but only 11% in group 1 and 15% in group 2 were considered allograft failures. Our failure rate is similar to the 18% failure rate reported in a systematic review when data of 19 articles on OCA transplantation in the knee were pooled.[5] A significantly higher reoperation rate was found in group 2. However, we believe that the longer follow-up time in group 2 may have influenced the higher reoperation rate in this group. Our population includes young and active adults with large and complex chondral and osteochondral lesions. This population is more susceptible to meniscal lesions, trauma, and new cartilage injuries, which explains our high reoperation rate in both groups of these highly demanding patients.

The treatment of a cartilage injury after a failed cartilage repair procedure has shown controversial outcomes in the literature. Zaslav et al,[29] in a multicenter, prospective study of the treatment of articular repair (the STAR study), included 154 patients with cartilage defect in the knee after a failed treatment of cartilage repair. Sustained and clinically meaningful improvement in pain and function after ACI was found at 48-month follow-up. The outcome was not different between patients whose primary procedure was marrow stimulation or simple debridement. However, the overall reoperation rate in this study was 49%, which is higher than other reports of primary ACI, suggesting an overall negative effect of previous surgeries. Minas et al[22] reported a failure rate 3 times that of nontreated defects in 321 consecutive patients treated with ACI after SMS. Recently, Nawaz et al[25] reported 1000 patients who had ACI for osteochondral defects in the knee; the investigators showed that 282 (34%) patients had a previous cartilage regenerative procedure, including Pride drilling, microfracture, and mosaicplasty. This group was 5 times more likely to have failure of ACI and demonstrated poorer clinical outcomes compared with patients treated with primary ACI. Beyond disagreement between studies, ACI appears to be sensitive to any damage of the environment of the subchondral bone plate or the subchondral bone caused by SMS. As previously described in the literature, SMS can cause a stiffer and harder subchondral plate, osseous overgrowth, and cystic formation that can influence the final outcome of ACI.[18,23]

We postulated that OCA transplantation is fundamentally different than ACI since the proper technique should remove the damaged subchondral bone during cartilage lesion preparation. Preparation requires a depth necessary to achieve a homogeneous bleeding surface of the subchondral bone, generally around 3 to 8 mm of depth.[27] The allograft is then prepared to replace the subchondral bone excised, explaining the tolerance of OCA transplantation to previous cartilage repair surgeries that compromise the subchondral bone. Gross et al[13] demonstrated the importance of subchondral bone in OCA transplantation. The authors performed histological studies on 35 allograft specimens after failure and concluded that features related to long-term allograft survival are dependent on graft stability by rigid fixation of host bone to graft bone. However, we believe that the damage to the subchondral bone caused by SMS can be completely substituted by the OCA transplant. This may explain our similar outcomes in both cohorts.

Our study is a comparative study but had several limitations. The study is a retrospective matched cohort study designed to assess the influence of previous cartilage repair, but it did not include a control group with another modality of treatment such as physiotherapy or different cartilage repairs for comparison. We used the modified Merle d'Aubigné-Postel score, which has not been validated for use in knees. This scoring system has been used since 1983, when no validated outcome scores were available. This scoring system has a simple score for pain and function that allows an intrasample comparison within the cohort. Currently, we are collecting IKDC, KOOS, and KS-F scores as well as the modified Merle d'Aubigné-Postel score. Another drawback was that we retrieved reoperation data via telephone for some of our patients and obtained clinical scores by mailed questionnaires. This method was used because our institution is a national referral center and many of our patients come from different regions and cannot return frequently for follow-up assessment. This study only included patients previously treated by SMS; our results cannot be extrapolated to patients who had other types of primary cartilage repair. Radiographic and magnetic resonance imaging documentation was not available in patients with long-term follow-up, so we could not assess early cases of osteoarthritis and allograft failures. However, image documentation in cartilage repair interventions does not seem to correlate precisely with functional outcomes.[2,9] Finally, there was a significant difference in follow-up duration between groups. This difference may explain the higher number of reoperations in group 2, since the patients had a longer follow-up time.

The treatments received by both groups proved to be reliable and effective options, as demonstrated by the improvements in pain and function, long survivorship, and high satisfaction rates without significant statistical differences between groups. Despite the higher reoperation rate in the previously treated group, previous cartilage repair did not affect the survivorship and functional outcome of OCA transplantation predominately in the femoral condyle of the knee. Thus, OCA transplantation is an appropriate treatment option for both primary repair of cartilage injuries and for revision of failed subchondral marrow stimulation.

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