Condyle-Specific Matching Does Not Improve Midterm Clinical Outcomes of Osteochondral Allograft Transplantation in the Knee

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Background: Condyle-specific matching for osteochondral allograft transplantation (OCA) pairs donor and recipient condyles in an attempt to minimize articular incongruity. While the majority of cartilage defects are located on the medial femoral condyle, lateral femoral condyles are more commonly available as a graft source. The purpose of this study was to compare the clinical outcomes of patients treated with non-orthotopic (lateral-to-medial condyle or medial-to-lateral condyle) OCA with those treated with traditional orthotopic (medial-to-medial condyle or lateral-to-lateral condyle) OCA. We hypothesized that clinical outcomes would be similar between groups at midterm follow-up.

Methods: A retrospective review of prospectively collected data on patients treated with OCA from 2000 to 2014 was conducted. Seventy-seven patients with a full-thickness cartilage defect of a femoral condyle were treated with either orthotopic (n = 50) or non-orthotopic (n = 27) OCA. A minimum follow-up of 2 years was required for analysis. Patients in each group were matched according to sex, age, and total chondral defect size. Reoperations and patient responses to validated outcome measures were reviewed. Failure was defined as any revision cartilage procedure or conversion to knee arthroplasty.

Results: The mean duration of follow-up was 4.0 years (range, 2 to 16 years). The orthotopic and non-orthotopic OCA groups were comparable in terms of demographics, the mean number of prior ipsilateral knee operations, and the percentage of concomitant procedures at baseline. Reoperation ($p = 0.427$) and failure ($p = 0.917$) rates did not differ significantly between groups. Both groups demonstrated significant increases in the Short Form-36 (SF-36) physical functioning and pain, International Knee Documentation Committee (IKDC), and Knee Outcome Survey-Activities of Daily Living (KOS-ADL) scores compared with baseline ($p < 0.004$). Outcome scores (baseline and postoperative) and change scores did not differ significantly between groups.

Conclusions: Clinical outcomes do not differ between patients treated with orthotopic OCA and those treated with non-orthotopic OCA, suggesting that condyle-specific matching may not be necessary.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Fresh osteochondral allograft transplantation (OCA) is a safe and effective procedure for the treatment of large articular cartilage lesions of the distal part of the femur[1,2]. This single-stage technique involves transfer of viable, mature hyaline cartilage and subchondral bone into chondral or osteochondral defects. Computer simulation and cadaveric studies have indicated that, while slightly recessed grafts can still restore contact pressures to nearly normal levels, grafts that are 0.5 to 1 mm proud can lead to substantial increases in contact pressures, making the graft prone to failure[3-5]. Thus, the goal for surgeons is to transplant the OCA plug with <1 mm of step-off from the surrounding recipient cartilage. To ensure optimal surface congruity, most surgeons attempt to match the donor and recipient femoral condyles in terms of size, laterality, and condyle (medial or lateral). Condyle-specific matching is performed because the morphometries of lateral and medial femoral condyles differ in shape, curvature, and size[6-8]. However, while full-thickness articular cartilage lesions are more common on the medial condyle than on the lateral condyle[9-11], 75% of the available graft supply is in the form of lateral condyles, presumably because of a higher incidence of arthrosis in the medial

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compartment[12,13]. As a result, condyle-specific matching restricts the number of compatible OCA grafts, and as many as 13% of harvested grafts are currently not utilized within the mandatory time frame[14].

Recent cadaveric laboratory studies have shown that non-orthotopic condyle grafts can achieve excellent surface matches when implanted into the recipient site[12,15]. In 1 study, 20-mm medial condyle defects filled with either medial or lateral condyle donor plugs exhibited overall height deviations of 0.63 mm for area and 0.47 mm for circumferential step-off, with no significant differences between medial and lateral condyle grafts[12]. In another study, investigators used the condyle radius of curvature as the sole matching criterion in a series of cadaveric distal femoral specimens and reported that the majority of the best-fit pairs, in terms of achieving minimal step-off, consisted of unmatched condyles[15]. While the aforementioned laboratory data suggest that non-orthotopic femoral condyle grafts may be suitable for defects in either condyle, the clinical effect and subsequent outcomes after lateral-to-medial condyle or medial-to-lateral condyle OCA are largely unknown.

The purpose of this study was to compare reoperation rates, failure rates, and patient-reported outcomes between patients treated with orthotopic OCA and those treated with non-orthotopic OCA. Our hypothesis was that the 2 treatment groups would have similar clinical outcomes at the time of midterm follow-up.

Materials and Methods

In 1999, our institution implemented a prospective registry dedicated to the tracking of patient outcomes after articular cartilage restoration procedures. An institutional review board approved the registry, and all patients sign an informed-consent form before participation. Patients included in the registry were evaluated preoperatively and were prospectively followed for up to 10 years postoperatively.

Inclusion and Exclusion Criteria

The inclusion criteria for the present study were (1) skeletal maturity, (2) symptomatic focal cartilage lesions of the medial or lateral femoral condyle classified as Outerbridge grade III or IV at the time of arthroscopic surgery and

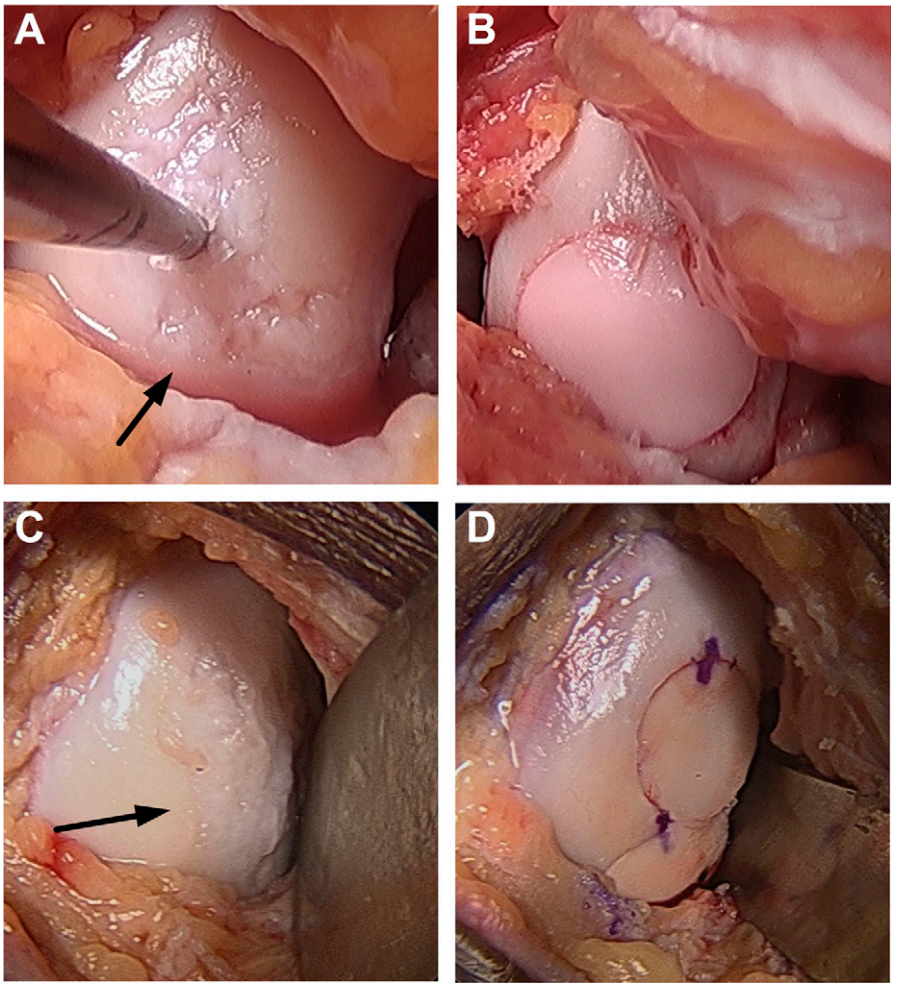

Fig. 1

Intraoperative photographs of OCA with a press-fit dowel technique after failed microfracture. **Figs. 1-A and 1-B** OCA with a single plug. **Figs. 1-C and 1-D** OCA using 2 plugs in a stacked fashion. The arrows indicate the cartilage defect after the failed microfracture.

TABLE I Similarity of Baseline Characteristics Between Study Groups

Patient Characteristics	Orthotopic (N = 50)	Non-Orthotopic (N = 27)	P Value
Sex (male/female) *(no.)*	30/20	19/8	0.459
Age* *(yr)*	35.4 (14-62)	35.9 (14-53)	0.851
Body mass index* *(kg/m²)*	25.5 (18-35)	26.8 (21-39)	0.228
No. of prior surgical procedures*	1.7 (0-10)	1.7 (0-4)	0.924
Follow-up* *(yr)*	4.4 (2-16)	3.4 (2-11)	0.025
Lesion characteristics			
Location *(%)*			<0.001
Medial femoral condyle	38	89	
Lateral femoral condyle	62	11	
Defect area* *(cm²)*	5.6 (2.3-10.5)	5.9 (2.3-8.0)	0.507
No. of plugs used*	1.4 (1-3)	1.4 (1-3)	0.692
Concomitant procedures *(no.)*			
ACL reconstruction†	2	4	0.176
Meniscal transplant	2	1	1.000
Realignment osteotomy	2	2	0.609

*The values are reported as the mean with the range in parentheses. †ACL = anterior cruciate ligament.

not involving substantial bone loss requiring additional bone-grafting, and (3) treatment with fresh OCA. To be eligible for analysis, patients were required to have a minimum of 2 years of follow-up. Exclusion criteria for OCA were generalized osteoarthritis, simultaneous multiligamentous reconstruction, inflammatory arthritis or an autoimmune condition, an age of <14 or >65 years, and an inability to comply with the postoperative rehabilitation protocol. Knees treated with tibial OCA were excluded as well.

Patients

Of the 1,870 registry patients screened, 122 treated consecutively between 2000 and 2014 met the inclusion and exclusion criteria. Of these 122 patients, 99 (99 knees) had a minimum of 2 years of follow-up. Graft records could not be located for 8 OCAs (6 of which were performed between 2000 and 2001). Therefore, 91 knees (75%) had complete data. One knee that had a prior total meniscectomy and was treated with staged OCA and meniscal transplantation 29 months apart as well as 8 knees treated by surgeons who performed only orthotopic OCA were excluded. Of the 82 knees eligible for analysis, 27 were treated with a hemicondyle allograft transplanted into the opposite recipient condyle (i.e., a non-orthotopic lateral-to-medial or medial-to-lateral condyle OCA). These knees were then matched to the remaining 55 knees treated with a hemicondyle allograft transplanted into the same condyle (i.e., an orthotopic medial-to-medial or lateral-to-lateral condyle OCA) on the basis of sex, age, and total chondral defect size. With 27 knees in the non-orthotopic group, 50 knees were required in the orthotopic group to achieve a power of ≥0.80 for demonstrating a minimal clinically important difference between the 2 groups with effect sizes of 0.87 (International Knee Documentation Committee [IKDC] score) and 0.72 (Knee Outcome Survey-Activities of Daily Living [KOS-ADL] score) and an alpha of 0.05[16,17]. Therefore, the 50 knees treated with orthotopic OCA that best matched the knees in the non-orthotopic group were included in the analysis. As a result, 77 knees in 77 patients were analyzed: 50 were treated with orthotopic OCA and 27, with non-orthotopic OCA.

Surgical Technique

All surgical procedures were performed by 2 fellowship-trained orthopaedic surgeons with extensive experience in cartilage repair procedures. Each surgeon performed both orthotopic and non-orthotopic OCA. After an examination with the patient under anesthesia, initial diagnostic arthroscopy of the joint was carried out for assessment of the chondral lesion as well as the other articular surfaces, menisci, and ligaments.

After the arthroscopic portion of the procedure, OCA was performed via the dowel technique described by Williams et al.[2]. Chondral lesions were exposed via a small parapatellar arthrotomy and debrided to a stable rim. Lesions were then sized and reamed to a bed of normal bone, and an appropriate graft was taken from the

TABLE II Reoperations After OCA

Procedure	No. of Knees*	
	Orthotopic	Non-Orthotopic
Arthroscopic chondroplasty/ loose body removal	5	3
Arthroscopic lysis of adhesions	1	1
Arthroscopic meniscal repair†	1	0
Implant removal	2	2
Irrigation and debridement	1	0
Manipulation under anesthesia	3	0
Open excision of infrapatellar scar	0	1
Revision cartilage restoration procedure	4	0
Unicompartmental knee arthroplasty	1	1
Total knee arthroplasty	2	1

*Some knees had >1 procedure during the reoperation or >1 reoperation. †Performed on the opposite side of the allograft.

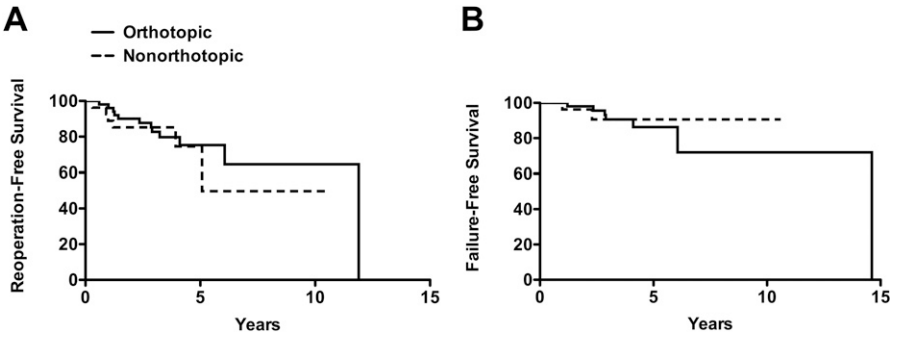

Fig. 2

Reoperation-free (**Fig. 2-A**) and failure-free (**Fig. 2-B**) survival of orthotopic and non-orthotopic OCA.

corresponding region of the hemicondyle allograft. Lesion depth was carefully measured at 4 points around the lesion, marked, and matched on the donor tissue. Grafts were then gently impacted into place for press-fit fixation. A single or dual circular dowel-shape graft was used in most cases, depending on lesion size (Fig. 1).

Fresh cold-stored osteochondral allografts were obtained from commercial sources. Donor tissue was screened and processed according to American Association of Tissue Banks standards[18]. Preoperatively, the donor and recipient femoral condyles were matched solely on the basis of size in the coronal dimension as measured on standard anteroposterior radiographs and/or magnetic resonance imaging (MRI). The condyles were not matched for side, whether they were medial or lateral, or their radius of curvature. Grafts were transplanted between 16 and 30 days after harvest depending on serologic testing and patient availability.

Postoperatively, patients were limited to touch-down or non-weight-bearing for a minimum of 1 to 2 weeks or, if they had been treated with concomitant meniscal transplantation or realignment osteotomy, for a minimum of 6 weeks. After 6 weeks, the postoperative protocols were similar for all patients. All participated in a supervised physical therapy program, with the duration dependent on the restoration of normal gait, return of quadriceps function, and performance of sport-specific skills. The return to higher-level activities and athletics was initiated on an individual patient basis and typically depended on a return of lower-extremity strength.

Assessment of Clinical Outcomes

All reoperations after the index OCA were documented. Failure of the allograft was defined as any subsequent revision cartilage procedure, unicompartmental knee arthroplasty, or total knee arthroplasty.

The general health outcome for each patient was assessed with use of the Short Form-36 (SF-36), version 1.0[19], which includes 8 domains of general well-being. Only the physical functioning, pain, and general health domains were assessed for this study. Knee function was assessed with use of the IKDC subjective form and the KOS-ADL. The IKDC score is a reliable and valid knee-specific measure of symptoms and function and has been shown to provide a good overall measure of knee-related disability in patients who have undergone a cartilage restoration procedure[20,21]. The KOS-ADL has been shown to have high reliability, validity, and responsiveness[22]. Patient activity level was assessed with use of the Marx Activity Rating Scale[23]. An independent observer collected the postoperative data with all clinical outcome instruments. These knee-specific outcome instruments have been used previously to evaluate cartilage restoration procedures in the knee[22,24-27].

Statistical Analysis

Comparisons of baseline patient characteristics between groups were conducted using independent-samples t tests for continuous variables and chi-square or Fisher exact tests for categorical variables. Kaplan-Meier survivorship analysis was performed for reoperations and failures, with comparisons between groups conducted using the log-rank test. Differences in subjective patient outcome scores between groups were assessed using independent-samples t tests. Changes in subjective patient outcome scores between preoperative and postoperative time points were assessed using paired-samples t tests. Two-tailed tests were used for all statistical analyses, with a critical α value set to 0.05.

Results

The mean duration of follow-up was 4.3 years overall: 4.4 years (range, 2 to 16 years) in the orthotopic group and 3.4 years (range, 2 to 11 years) in the non-orthotopic group ($p = 0.025$). Patient demographics, chondral lesion characteristics, and

TABLE III Comparison of Preoperative and Postoperative Outcome Scores Between Study Groups

	Preoperative			Postoperative		
	Mean ± SD *(points)*			Mean ± SD *(points)*		
	Orthotopic	Non-Orthotopic	P Value*	Orthotopic	Non-Orthotopic	P Value*
SF-36 physical functioning	58.6 ± 21.8	59.8 ± 25.6	0.859	83.6 ± 18.1	83.8 ± 12.4	0.964
SF-36 pain	63.0 ± 78.5	51.3 ± 18.4	0.330	75.0 ± 23.4	71.5 ± 19.4	0.538
SF-36 general health	75.5 ± 16.0	75.0 ± 19.0	0.912	80.1 ± 16.1	77.0 ± 19.4	0.536
IKDC	47.0 ± 13.7	45.8 ± 13.7	0.738	66.6 ± 21.0	70.4 ± 17.0	0.434
KOS-ADL	65.9 ± 14.0	61.5 ± 15.8	0.270	83.4 ± 12.7	84.1 ± 11.9	0.828
Marx Activity Rating Scale	6.5 ± 6.6	4.8 ± 5.3	0.250	4.6 ± 4.7	4.7 ± 4.8	0.915

*Comparisons were made using the independent-samples t test.

TABLE IV Change Scores for Each Study Group

	Orthotopic		Non-Orthotopic		
	Mean ± SD *(points)*	P Value*	Mean ± SD *(points)*	P Value*	Group-Difference P Value†
SF-36 physical functioning	23.6 ± 23.2	<0.001	19.7 ± 21.6	0.002	0.545
SF-36 pain	22.4 ± 26.2	<0.001	23.7 ± 27.6	0.003	0.876
SF-36 general health	4.1 ± 18.1	0.158	3.2 ± 11.0	0.244	0.821
IKDC	20.7 ± 17.2	<0.001	23.3 ± 18.2	<0.001	0.590
KOS-ADL	15.9 ± 11.8	<0.001	23.8 ± 18.7	<0.001	0.108
Marx Activity Rating Scale	−1.4 ± 4.3	0.039	−0.3 ± 3.7	0.653	0.304

*Comparisons between preoperative and postoperative scores using the paired-samples t test. †Comparisons of change scores between the orthotopic and non-orthotopic groups using the independent-samples t test.

the proportions of patients undergoing concomitant procedures were similar between groups (Table I). The mean number of prior surgical procedures on the ipsilateral knee was 1.7 in both groups ($p = 0.924$). Seventeen knees (34%) in the orthotopic group and 9 knees (33%) in the non-orthotopic group had previously undergone a cartilage restoration procedure, including microfracture (n = 19), mosaicplasty (n = 2), autologous chondrocyte implantation (n = 2), and use of a synthetic scaffold (n = 3). The percentage of medial condyle defects was higher in the non-orthotopic group than in the orthotopic group since 70% of the transplanted allografts were derived from lateral condyles. Over the study period, transplanted allografts were obtained from 4 tissue banks, including the Musculoskeletal Transplant Foundation (88%), Joint Restoration Foundation (5%), CryoLife (4%), and University of Miami Tissue Bank (3%).

Reoperations and Failures

At the time of final follow-up, 20 (26%) of the knees had undergone a reoperation after the OCA (Table II). Five knees (10%) in the orthotopic group and 3 knees (11%) in the non-orthotopic group underwent arthroscopic chondroplasty or loose body removal after the OCA ($p = 1.000$). For 4 of these procedures (2 in each group), the chondroplasty was performed in areas outside the previously grafted compartment and the allograft was seen to be fully intact. Failures were documented in 9 knees (12%). The overall mean time to failure (and standard deviation [SD]) was 4.2 ± 4.2 years. OCA survivorship was 98% at 2 years and 86% at 5 years for the orthotopic group and 96% at 2 years and 91% at 5 years for the non-orthotopic group. The reoperation ($p = 0.427$) and failure ($p = 0.917$) rates did not differ significantly between groups (Fig. 2).

Outcome Scores

No significant differences in the physical functioning, pain, or general health scores of the SF-36 or in the IKDC, KOS-ADL, or Marx Activity Rating Scale scores were detected between the groups at the preoperative or postoperative time points (Table III). The scores on the postoperative physical functioning and pain subscales of the SF-36 and the IKDC and KOS-ADL scores improved significantly from the preoperative values in both groups ($p < 0.004$) (Table IV). The change scores for the IKDC and KOS-ADL in both groups were above the minimal clinically important difference reported for each instrument (16.7 for the IKDC and 10.6 for the KOS-ADL)[16,17]. In the orthotopic group, the change in the Marx Activity Rating Scale score (−1.4 ± 4.3) was significant ($p = 0.039$) but probably not clinically important. The change in the SF-36 general health subscale score was not significant ($p \geq 0.158$) in either group. Comparison of change scores between the orthotopic and non-orthotopic groups revealed no significant differences ($p > 0.100$).

Discussion

While the number of OCAs has increased dramatically in recent years, many harvested allografts are not utilized until immediately before expiration and as many as 13% of available allografts are discarded[14]. This is due in part to the matching constraints employed by many surgeons, which include pairing donor-recipient size, laterality, and condyle. The difficulty in finding a suitable match is exacerbated by the fact that articular cartilage lesions are approximately 6 times more common on the medial condyle than on the lateral condyle[9-11] while 75% of available grafts are from lateral condyles[12]. The results of our study demonstrate that clinical outcomes after non-orthotopic OCA are similar to those after orthotopic OCA, suggesting that condyle-specific matching may not be necessary.

Conventional size, laterality, and condyle-specific matching are thought to minimize graft-recipient articular incongruity. Biomechanical and computer simulation studies have indicated that cylindrical grafts elevated 0.5 to 1 mm above the adjacent cartilage can lead to as much as a 50% increase in contact pressures[3-5,28,29]. However, many factors contribute to condyle geometry, and it may be overly simplistic to assume that a conventionally matched orthotopic allograft will ensure a smooth surface contour at the recipient site. Our results corroborate those from a cadaveric study by Mologne et al.[12], in which 20-mm medial condyle defects were filled with either

medial femoral condyle or lateral femoral condyle graft and the resultant topography was compared. The authors observed that both the medial and the lateral condyle donor grafts were associated with <1 mm of articular step-off (proud or recessed) along at least 95% of their circumference, and only 12% of the implant areas were proud. There were no significant differences in height deviation for area or step-off between the medial and lateral condyle grafts. Thus, Mologne et al. concluded that lateral femoral condyle allografts are acceptable options for medial condyle defects.

In another cadaveric study, the investigators examined the radius of curvature as a singular matching criterion for donor-recipient pairing[15]. Seven optimal donor-host pairs were identified from 14 randomly selected distal femoral hemicondyles. Five of the 7 matches were non-orthotopic (lateral-to-medial or medial-to-lateral condyle). A 25-mm OCA was then performed with each of the identified pairs, and the step-offs for all plugs were <1 mm from the recipient articular surface. Using the radius-of-curvature matching methodology, these investigators similarly identified acceptable non-orthotopic matches for simulated 20 and 30-mm defects in small, medium, and large knees. Compared with conventional matching, this method yielded a 3.2-fold greater match rate for both medial and lateral femoral condyle lesions, suggesting that condyle-specific matching limits the number of available matches.

The surgeon's ability to resurface a defect with minimal step-off depends not only on the surface topographies of the recipient and donor condyles, but also on the angle and depth (with respect to the articular surface) of the harvested osteochondral plug compared with that of its recipient socket. Slight deviations from the perpendicular of the articular surface and variances in the circumferential depth can lead to a proud or recessed graft. While performing an OCA, we tend to accept a transplanted graft that exhibits up to 1.0 to 1.5 mm of depression because additional attempts to improve the surface contour through repeated manipulation and impaction risk more chondrocyte death and changes to the mechanical properties of the graft[30]. Although surgeons strive to achieve the "perfect" fit, in reality a slight step-off is common and sometimes unavoidable after OCA.

We believe that we are the first to report no difference in failure rates or subjective outcomes between orthotopic and non-orthotopic femoral condyle OCA, and this finding has several clinical implications. If surgeons forewent condyle-specific matching, more allografts would be readily available, which would shorten wait times, provide fresher grafts with increased chondrocyte viability, and lower procedure costs. Fewer grafts would have extended storage times or be discarded. Several prior studies have shown that donor-cell viability decreases with storage time[31,32] and that viability at the time of transplantation is linked to successful outcomes[33]. Moreover, if medial-lateral dimension is the only criterion used in the matching process, as was the case for the patients in this study, then lateral condyles are an optimal graft source for defects on either condyle. Lateral condyles are generally wider than medial condyles, so they can be used to treat larger lesions. It was reported that 75% of available grafts that are wider than 25 mm in the coronal dimension are lateral femoral condyles[12]. Additionally, lateral femoral condyles generally have thicker cartilage and a higher tensile modulus and strength than corresponding areas on the medial condyle[34,35].

There are several limitations to our study. As with any retrospective study, the patients were not randomized to the treatment groups, which may have introduced selection bias. Despite the lack of randomization, the 2 patient groups had comparable demographics and baseline scores. Age and the number of prior surgical procedures on the ipsilateral knee, which have been shown to influence outcomes of OCA[36,37], were similar between groups. Articular congruity at the graft-host junction, which affects load transmission on the recipient condyle and is important to the success of the OCA transplantation[38,39], was not quantified intraoperatively or directly evaluated with immediate postoperative MRI, as these approaches are currently not the standard of care. Additionally, this study did not include standardized follow-up physical examination or imaging findings.

Another limitation is the midterm duration of follow-up, as femoral condyle OCAs typically fail at an average of 3 to 7 years after surgery[36,37,40-42]. However, given the marked similarities between the 2 treatment groups, longer follow-up is unlikely to show a significant difference—and especially unlikely to show a minimal clinically important difference—in the postoperative outcome scores between the 2 groups. Finally, both groups included patients who had concomitant procedures, the effects of which are relatively unknown. However, multiple studies have demonstrated favorable outcomes following OCA combined with meniscal transplantation or osteotomy[28,42-45], and there were no differences in the proportions of patients with concomitant procedures between our groups.

In conclusion, both orthotopic and non-orthotopic OCA resulted in significantly improved outcomes at the time of midterm follow-up. Failure rates and patient-reported outcomes did not differ between the 2 groups. These results suggest that surgeons can forgo condyle-specific matching, which would make osteochondral allografts much more readily available. ■

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