Osteochondral Allograft Transplantation of the Knee in Patients Aged 40 Years and Older

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Background: Treatment of large chondral defects of the knee among patients aged ≥40 years remains a difficult clinical challenge owing to preexisting joint degeneration and the lack of treatment options short of arthroplasty.

Purpose: To characterize the survivorship, predictors of failure, and clinical outcomes of osteochondral allograft transplantation (OCA) of the knee among patients aged ≥40 years.

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

Methods: Prospectively collected data were reviewed for 54 consecutive patients aged ≥40 years who were treated with OCA. Preoperative levels of osteoarthritis (according to Kellgren-Lawrence classification) and meniscal volume and quality were graded from review of radiographs and magnetic resonance imaging. Complications, reoperations, and patient responses to validated outcome measures were reviewed. A minimum follow-up of 2 years was required for analysis. Failure was defined by any removal or revision of the allograft or conversion to arthroplasty.

Results: Among 51 patients (mean age, 48 years; range, 40-63 years; 65% male), a total of 52 knees had symptomatic focal cartilage lesions (up to 2 affected areas) that were classified as Outerbridge grade 4 at the time of OCA and did not involve substantial bone loss requiring shell allografts or additional bone grafting. Mean duration of follow-up was 3.6 years (range, 2-11 years). After OCA, 21 knees (40%) underwent reoperation, including 14 failures (27%) consisting of revision OCA (n = 1), unicompartmental knee arthroplasty (n = 5), and total knee arthroplasty (n = 8). Mean time to failure was 33 months, and 2- and 4-year survivorship rates were 88% and 73%, respectively. Male sex (hazard ratio = 4.18, 95% CI = 1.12-27.13) and a higher number of previous ipsilateral knee operations (hazard ratio = 1.70 per increase in 1 surgical procedure, 95% CI = 1.03-2.83) were predictors of failure. A higher Kellgren-Lawrence osteoarthritis grade on preoperative radiographs was associated with higher failure rates in the Kaplan-Meier analysis but not the multivariate model. At final follow-up, clinically significant improvements were noted in the pain (mean score, 47.8 to 67.6) and physical functioning (56.8 to 79.1) subscales of the Short Form-36, as well as the International Knee Documentation Committee subjective form (45.0 to 63.6), Knee Outcome Survey–Activities of Daily Living (64.5 to 80.1), and overall condition statement (4.5 to 6.8) ($P < .001$). No significant changes were noted for the Marx Activity Rating Scale (5.1 to 3.9, $P = .789$).

Conclusion: A higher failure rate was found in this series of patients aged ≥40 years who were treated with OCA as compared with other studies of younger populations. However, for select older patients, OCA can be a good midterm treatment option for cartilage defects of the knee.

Keywords: osteochondral allograft; age; cartilage; knee arthroplasty; clinical outcomes

Cartilage restoration procedures have demonstrated good results for young patients, as evidenced by improved pain and function as well as a high rate of return to sporting activities.[20,21] In contrast, the outcomes for older patients have not been as encouraging. Several studies showed that patients aged ≥30 years have less favorable outcomes when compared with those <30 years of age.[5,18,24] This discrepancy may be attributed to the larger articular defects and concomitant meniscal, chondral, and subchondral disease seen more frequently among older patients.[4] As a result, some authors indicated an age of 40 to 50 years as a relative contraindication to cartilage repair.[3,37]

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The treatment of large chondral defects of the knee among patients aged ≥40 years continues to be a difficult clinical challenge. For these middle-aged patients, traditional arthroplasty continues to be a poor option, owing to implant longevity concerns, particularly among patients <50 years of age.[16,33] Fresh osteochondral allograft transplantation (OCA) has recently been advocated for the treatment of large chondral defects. This procedure has demonstrated 5- and 10-year survival rates of 89% and 82%, respectively, and although reoperation rates are approximately 40%, patient satisfaction remains high.[9,23] OCA is particularly suitable in older patients because of the single-stage transfer of viable mature hyaline cartilage into chondral defects while avoiding donor site morbidity, allowing for a faster rehabilitation than that of other cartilage repair strategies. However, current evidence is limited on the clinical outcomes of OCA for older patients.

The purpose of this study was to characterize the clinical results of OCA among patients aged ≥40 years as demonstrated by graft survivorship and patient-reported outcomes. For this cohort of older patients, we sought to identify the predictors for graft failure. We hypothesized that older age, a higher number of previous ipsilateral knee operations, and preexisting joint degeneration would be associated with higher failure rates, while clinically significant improvements in patient-reported outcomes would be observed after OCA.

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 then prospectively followed at 1, 2, 3, 4, 5, and 10 years postoperatively.

Inclusion and Exclusion Criteria

Inclusion criteria included (1) age ≥40 years, (2) symptomatic focal cartilage lesions (up to 2 affected areas) in the knee that were classified as Outerbridge grade 4 lesions at the time of OCA and did not involve substantial bone loss requiring shell allografts or additional bone grafting, (3) treatment with fresh osteochondral allograft, and (4) a minimum of 2 years of follow-up. Exclusion criteria for this cartilage procedure were advanced osteoarthritis (OA), simultaneous multiligamentous reconstruction, inflammatory arthritis or autoimmune conditions, and inability to comply with the postoperative rehabilitation protocol.

Patients

Demographic and pre-, intra-, and postoperative data were collected for all patients. Demographic data included age, sex, and body mass index (BMI). Preoperative data included the number and type of previous ipsilateral knee operations and baseline patient-reported outcome scores. 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 depended on the surgeon's practice; for the majority of patients, long-leg radiographs were obtained only if gross malalignment was detected and osteotomy was being considered. Intraoperative data included laterality; results of examination under anesthesia (range of motion, ligamentous stability); location, size and depth of the chondral defect(s); status of the articular surfaces in other compartments; meniscus status; and concomitant procedures performed. Postoperative data included rehabilitation protocol, complications, reoperations, and patient-reported outcome scores at a minimum of 2 years after surgery.

Osteoarthritis and Meniscus Scoring

Predetermined scoring systems (Table 1) were used to assign grades indicative of the degree of OA (OA grade), meniscal volume in the transplanted compartment (meniscus volume grade), and meniscal quality in the transplanted compartment (meniscal quality grade) for each patient. OA grades were assigned with the Kellgren-Lawrence grading system based on retrospective review of preoperative radiographs.[17] For a small subset of patients for which preoperative radiographs were not available, immediate postoperative radiographs or preoperative magnetic resonance imaging (MRI) was reviewed. Only intra-articular areas outside the focal chondral defect were evaluated. Meniscal volume and quality grades were formulated from the retrospective review of preoperative MRI. All scoring was performed by a fellowship-trained musculoskeletal radiologist (V.K.) blinded to the outcomes.

Surgical Indications for OCA

Fresh OCA was selected as the treatment option for these patients based on clinical judgment of defect complexity, defect size, and failure of previous surgical or nonsurgical treatments. Generally, OCA was performed for focal full-thickness chondral defects ≥2 cm^2 diagnosed on MRI or prior arthroscopy. Prior failure of other cartilage restoration procedures (eg, microfracture) was not a contraindication. Autologous chondrocyte implantation (ACI) was rarely performed at this study's institution, owing to its 2-stage process and slower rehabilitation when compared with that for osteochondral grafting.

Surgical Technique

All surgical procedures were performed at a single institution by 2 fellowship-trained orthopaedic surgeons (R.J.W. and S.A.R.) 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

TABLE 1
Osteoarthritis and Meniscus Scoring Criteria

Osteoarthritis/Meniscus: Grades	Criteria
Osteoarthritis	
1	Doubtful—minute osteophyte, doubtful significance
2	Minimal—definite osteophyte, no joint space narrowing
3	Moderate—moderate joint space narrowing
4	Severe—severe joint space narrowing and subchondral sclerosis
Ipsilateral meniscal volume	
1	Intact meniscus and no evidence of previous partial meniscectomy
2	>50% meniscus left after previous partial meniscectomy
3	<50% meniscus left
4	Little or no meniscus left
Ipsilateral meniscal quality	
1	Normal meniscus signal and morphology
2	Intrameniscal signal hyperintensity, normal morphology
3	Intrameniscal signal hyperintensity, abnormal morphology
4	Intrameniscal signal hyperintensity, indistinctness, scarring

other articular surfaces, menisci, and ligaments. Any meniscal tears were addressed with partial meniscectomy or repair.

Fresh cold-stored osteochondral allografts were obtained from commercially available sources. Donor tissue was screened and processed according to standards per the American Association of Tissue Banks.[27] Preoperatively, donor and recipient were matched on the basis of size via standard anteroposterior radiographs. Grafts were transplanted between 16 and 30 days after harvest, depending on serologic testing and patient availability. After the arthroscopic portion of the procedure, OCA was performed via the dowel technique described by Williams et al.[38] Briefly, chondral lesions were exposed through a small parapatellar arthrotomy without patellar eversion 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 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. Grafts were a single or dual circular dowel shape in most cases, depending on lesion shape.

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 thereafter, depending on return of lower extremity strength.

Assessment of Clinical Outcomes

All complications and reoperations after the index OCA were documented. A reoperation was defined as any subsequent surgery on the ipsilateral knee, including arthroscopic chondroplasty, removal of loose bodies, lysis of adhesions, and hardware removal. Failure of the allograft was defined as any procedure that involved removal or revision of the allograft, unicompartmental knee arthroplasty, or total knee arthroplasty.

The general health outcome for each patient was assessed with the Short Form–36 (SF-36; v 1.0),[29] which has the ability to evaluate 8 domains of general well-being. The only domains reported in this study were general health, pain, physical functioning, and role limitations attributed to physical health. Knee function was assessed with the International Knee Documentation Committee subjective form (IKDC) and the Knee Outcome Survey–Activities of Daily Living (KOS-ADL). The IKDC score is a reliable and valid knee-specific measure of symptoms and function and provides a good overall measure of knee-related disability among patients who have undergone a cartilage restoration procedure.[13,15] Similarly, the KOS-ADL has high reliability, validity, and responsiveness for athletic patients with various knee conditions.[25] Patient activity level was assessed with the Marx Activity Rating Scale.[26] Finally, the overall condition of the knee was assessed with the patient perception component of the Cincinnati Knee Rating System.[2] This single item, "Rate the overall condition of your knee at the present time," is based on a scale of 1 to 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."[2] An independent observer performed postoperative data collection for all clinical outcome instruments. All these knee-specific outcome instruments have been used to prospectively evaluate articular cartilage repair procedures of the knee.[20,21,25,35,36]

Statistical Analysis

Kaplan-Meier survivorship analysis was performed for failures, with comparisons among groups conducted with the

TABLE 2
Patient Demographics and Concomitant Surgery[a]

	All Knees (n = 52)[b]	Failures (n = 14)
Patient characteristics		
Age, y	48.0 (40-63)	50.8 (43-63)
Sex, male:female	33:18	12:2
Body mass index, kg/m^2	26.6 (20-38)	26.2 (22-34)
Laterality, right:left	26:26	7:7
Preoperative Marx Activity Rating Scale	5.1 (0-14)	5.3 (0-13)
No. of previous surgical procedures	1.4 (0-4)	2.0 (1-4)
Lesion characteristics		
OCA location		
Medial femoral condyle	30 (58)	9 (64)
Lateral femoral condyle	14 (27)	2 (14)
Trochlea	16 (31)	6 (43)
Patella	7 (13)	2 (14)
Chondral defect area, cm^2	6.5 (0.8-15.3)	6.5 (3.8-9.5)
No. of plugs used	1.9 (1-3)	2.2 (1-3)
Concomitant procedures		
Revision ACLR	2	1
Meniscus allograft transplantation	1	0
Realignment osteotomy	2	0

[a]Data are reported as mean (range) or n (%). ACLR, anterior cruciate ligament reconstruction; OCA, osteochondral allograft transplantation.
[b]Fifty-one patients (1 patient had OCA in bilateral knees).

log-rank test. Multivariable proportional hazards regression modeling with backward selection and a threshold *P* value <.20 identified those factors that were best predictive of failure. Factors initially entered into the model included age, sex, BMI, pre- and postoperative Marx Activity Rating Scale scores, number of previous ipsilateral knee operations, chondral defect area and primary location, OA grade, and meniscal volume and quality grades. Comparisons among factors were performed with the Mann-Whitney test for binary characteristics, chi-square or Fisher exact tests for discrete variables, and bivariate correlations for continuous variables. Changes in subjective patient outcome scores (SF-36, IKDC, KOS-ADL, Marx Activity Rating Scale, and overall condition) between pre- and postoperative time points were assessed with the Wilcoxon signed-rank test. Two-tailed tests were used for all statistical analyses, with a critical *P* value set to .05 to indicate significance.

RESULTS

Of the 1902 registry patients screened, 54 (3%) consecutive patients treated between 2000 and 2014 met the inclusion and exclusion criteria. Three patients were lost to follow-up. As a result, 52 knees (n = 51 patients) were analyzed (94% follow-up). The mean age was 48 years (range, 40-63 years). Sixteen patients (31%) were ≥50 years old at the time of surgery. Mean duration of follow-up was 3.6 years (range, 2-11 years). Table 2 presents patient demographics, chondral lesion characteristics, and concomitant procedures.

Fourteen knees (27%) had previously undergone a cartilage restoration procedure, including microfracture (n = 10), OCA (n = 1), ACI (n = 1), and synthetic scaffold (n = 2). Twelve knees (23%; n = 12 patients) had previously undergone anterior cruciate ligament reconstruction. Documented Lachman and pivot-shift grades at the time of examination under anesthesia were 1A and 0, respectively, for 10 of these patients who did not have any symptoms or signs of graft failure. The other 2 patients had positive signs of graft failure preoperatively and were treated with combined OCA and revision anterior cruciate ligament reconstruction. Five knees (10%) were treated with bipolar OCA for reciprocal lesions in the patellofemoral joint, and 2 knees (4%) were treated with isolated patella OCA. One knee (2%) had a prior subtotal lateral meniscectomy and thus was treated with a combined lateral meniscus allograft transplantation and lateral femoral condyle OCA. One knee (2%) was treated with a combined high tibial osteotomy and medial femoral condyle OCA for isolated medial compartmental disease, and 1 knee (2%) was treated with a combined tibial tubercle osteotomy and patella OCA for lateral patellar overload.

Preoperative radiographs were available for 40 (77%) knees. For the remaining knees, Kellgren-Lawrence OA scoring was based on preoperative MRI or immediately postoperative radiographs. The mean OA grade was 1.9 ± 0.8. For patients who received condylar OCAs (excluding 1 patient who received a concomitant meniscus transplant), the mean meniscal volume and quality grades were 2.5 ± 0.7 and 2.8 ± 0.6, respectively. No patients had a meniscal volume or quality grade of 4. Higher OA grade, indicating more overall degeneration, was correlated with higher meniscal volume grade ($R = -0.36$, $P = .016$) but not meniscal quality grade ($P = .936$). Increasing age was correlated with higher meniscal volume grade ($R =$

TABLE 3
Reoperations After OCA[a]

Procedure	No.[b]
Arthroscopic chondroplasty/loose body removal	7
Arthroscopic lysis of adhesions	1
Arthroscopic meniscectomy	2
Arthroscopic meniscal repair	1
Irrigation and debridement	2
Hardware removal	2
Open excision of infrapatellar scar	1
Revision OCA[c]	1
Unicompartmental knee arthroplasty[c]	5
Total knee arthroplasty[c]	8

[a]OCA, osteochondral allograft transplantation.
[b]Some knees had >1 procedure during reoperation or >1 reoperation.
[c]Failures.

−0.34, P = .020) and quality grade (R = −0.49, P = .005) but not OA grade (P = .358).

Complications, Reoperations, and Failures

Four knees (8%) developed arthrofibrosis postoperatively and were treated with manipulation under anesthesia (n = 2) or lysis of adhesions/scar excision (n = 2). No superficial or deep infections were observed in the initial postoperative period after OCA. Two knees (4%) developed deep infections after subsequent reoperations. One developed a postoperative septic joint after an arthroscopic lysis of adhesions, which was treated with arthroscopic irrigation and debridement. This patient underwent a total knee arthroplasty in the same knee 45 months after the arthroscopic irrigation and debridement. A patient who had a concomitant opening-wedge high tibial osteotomy developed a deep tibial wound infection after staged removal of the osteotomy plate, which was treated with irrigation and debridement and local fasciocutaneous advancement flap coverage. At final follow-up, this patient was doing well and did not require any subsequent procedures.

In total, 21 knees (40%) underwent reoperation after OCA (Table 3). Seven knees (13%) underwent arthroscopic chondroplasty and/or loose body removal after OCA. Failures were documented for 14 knees (27%), as defined by revision OCA (n = 1), unicompartmental knee arthroplasty (n = 5), and total knee arthroplasty (n = 8). The mean time to failure was 33 months (range, 11-82 months). Kaplan-Meier survival analysis demonstrated 88% survivorship at 2 years and 73% at 4 years (Figure 1). Comparison of survival among patients grouped by demographic factors and joint degeneration scores revealed statistically significant differences among sex (P = .034), number of previous ipsilateral knee operations (P = .019), and OA grade (P = .007) (Figure 2). Comparisons of survival among patients grouped by meniscal volume or quality grade demonstrated no significant differences (P > .106). Multivariable proportional hazards regression revealed that male sex

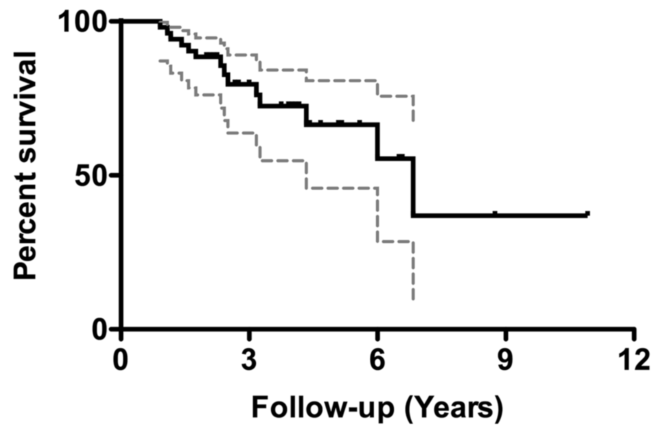

Figure 1. Osteochondral allograft transplantation survivorship among patients aged ≥40 years. Dotted lines indicate 95% CI.

(P = .032, hazard ratio = 4.18, 95% CI = 1.12-27.13) and a higher number of previous ipsilateral knee operations (P = .037, hazard ratio = 1.70 per increase in 1 surgical procedure, 95% CI = 1.03-2.83) were predictors of failure (Table 4).

Outcome Scores

Six patients (12%) experienced failure of their OCA within 2 years of their index procedure. Of the remaining 45 patients, 40 (89%) had complete responses to outcome measures at their most recent follow-up. Postoperatively, statistically significant improvements were noted in the pain, physical functioning, and role limitations subscales of the SF-36, as well as the IKDC, KOS-ADL, and overall condition statement (P < .001 for all) (Table 5).

DISCUSSION

The principal findings of this study of OCA in patients aged ≥40 years were as follows: (1) allograft survivorship was 88% at 2 years and 73% at 4 years; (2) a higher number of previous ipsilateral knee operations and male sex were significant predictors of failure, while higher Kellgren-Lawrence OA grade was associated with higher failure rates in the Kaplan-Meier analysis but not the multivariate model; and (3) OCA resulted in clinically significant improvements in knee symptoms and function, as indicated by validated outcome measures.

The current evidence on cartilage restoration procedures suggests that older age is correlated with higher failure rates and less improvement in outcomes.[5,11,18,23,24,31] Prior studies performed matched comparisons between older and younger cohorts of patients, and the majority showed at least a tendency toward worse outcomes for older patients.[10,32] This is not surprising given the degenerative processes and declining healing potential that progress with age. As a result,

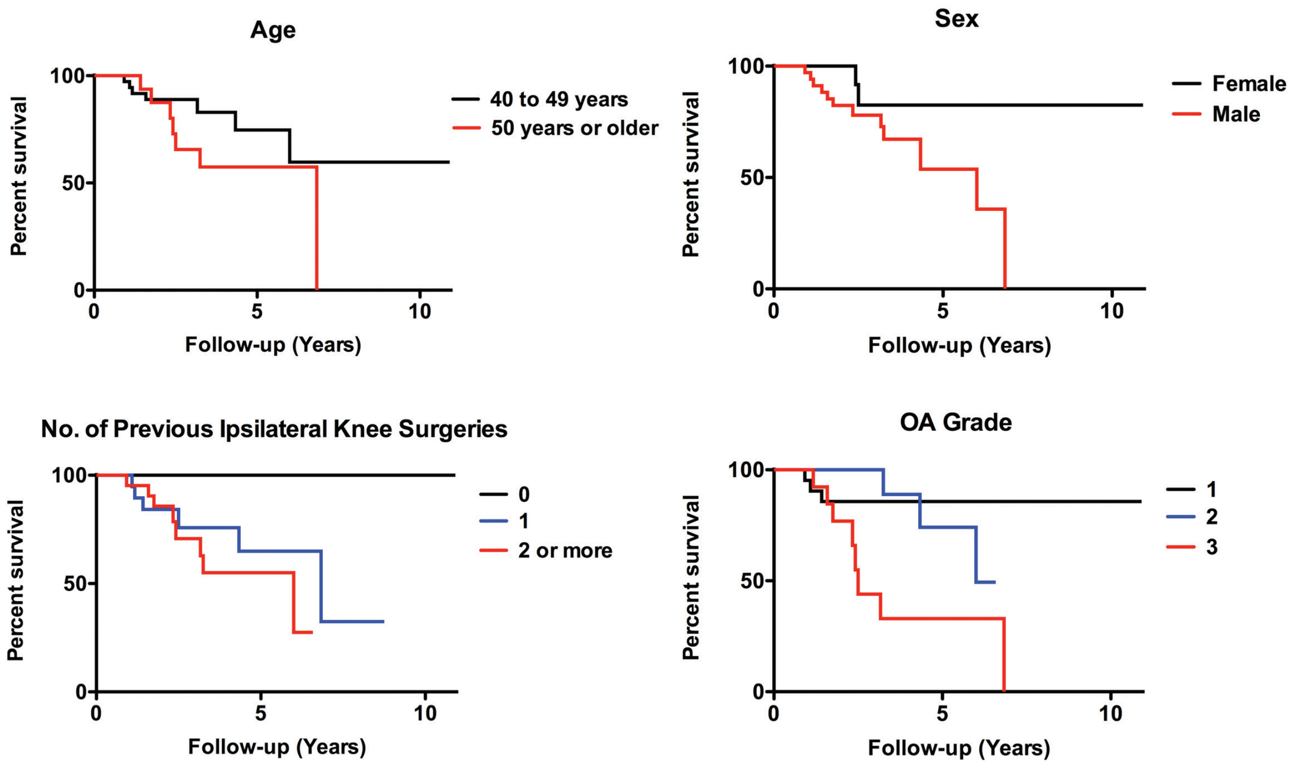

Figure 2. Osteochondral allograft transplantation survivorship among patients grouped by age, sex, number of previous ipsilateral knee operations, and Kellgren-Lawrence osteoarthritis (OA) grade. P = .136 for age, P = .034 for sex, P = .019 for number of previous ipsilateral knee operations, and P = .007 for OA grade.

TABLE 4
Multivariable Regression of Predictors of OCA Failure[a]

Covariate	Hazard Ratio[b]	95% CI	P Value
Sex, male:female	4.18	1.12-27.13	.032
No. of previous surgical procedures	1.70	1.03-2.83	.037
Kellgren-Lawrence OA grade	1.67	0.80-3.59	.172

[a]OA, osteoarthritis; OCA, osteochondral allograft transplantation.
[b]Values represent hazard ratio per unit increase unless otherwise indicated.

some authors have recommended an age limit of 40 to 50 years for cartilage restoration procedures.[3,37] However, this line of thinking may be shortsighted, as significant improvements in outcomes are consistently seen for patients aged ≥40 years among all cartilage restoration procedures, including microfracture, ACI, and osteochondral autograft transfer (OAT).[1,6,19,22,32,34] Similarly, we found that patients aged ≥40 years reported clinically significant improvement in outcomes after OCA. In a study of patients aged ≥45 years who were treated with ACI, 72% reported their outcomes as good or excellent, and 81% would choose to undergo ACI again despite 43% undergoing repeat knee arthroscopy after the ACI procedure.[34] Clearly, high satisfaction can be achieved among older patients after cartilage repair. Additionally, older patients should not be assessed in the same manner as younger, more active patients. Whereas the primary goal of younger patients undergoing cartilage repair may be to return to high-impact sports, the goals of older patients may be more related to pain relief and an improved ability to perform low-impact physical or daily activities.[10] The results of our study suggest as much: Marx Activity Rating Scale scores stayed constant, at a mean of 4 to 5 (indicating low levels of physical activity), while pain and daily functioning scores significantly improved after OCA. Rather than comparing the results of older versus younger patients after such procedures, studies should attempt to identify the predictors of success and failure in the older population. Certainly, this would help clinicians distinguish the ideal candidates from those prone to early failure after cartilage restoration surgery.

OCA is a particularly attractive option for older patients because of the single-stage transfer of viable mature hyaline cartilage into chondral defects, which allows for a quicker rehabilitation than that of ACI and which avoids the donor site morbidity associated with OAT. However, the current evidence on the outcomes of OCA for older patients is limited. Degen et al[6] reported on 61 patients aged ≥40 years who were treated with OAT, OCA, or synthetic scaffold plugs. The mean defect size by procedure was 3.3 cm^2 for OAT, 5.8 cm^2 for OCA, and 3.2 cm^2 for synthetic scaffolds. All treatments resulted in significant improvements in outcome scores. However, limited conclusions can be drawn from this study owing to the lack of

TABLE 5
Preoperative, Postoperative, and Change Outcome Scores at Final Follow-up[a]

Measure	Score			
	Preoperative	Postoperative	Change	*P* Value[b]
SF-36				
General health	72.3 ± 15.1	76.3 ± 17.8	4.4 ± 18.4	.185
Pain	47.8 ± 22.8	67.6 ± 26.9	20.7 ± 22.5	<.001
Physical functioning	56.8 ± 22.5	79.1 ± 20.1	23.5 ± 23.0	<.001
Role limitations per physical health	45.3 ± 42.0	78.6 ± 36.0	33.3 ± 41.3	<.001
IKDC	45.0 ± 14.2	63.6 ± 19.6	19.2 ± 18.3	<.001
KOS-ADL	64.5 ± 14.5	80.1 ± 13.8	15.2 ± 12.7	<.001
Marx Activity Rating Scale	5.1 ± 5.3	3.9 ± 4.2	–0.6 ± 4.4	.789
Overall condition	4.5 ± 1.5	6.8 ± 1.8	2.4 ± 2.4	<.001

[a]Values represent mean ± SD points. IKDC, International Knee Documentation Committee Subjective Knee Evaluation Form; KOS-ADL, Knee Outcome Survey–Activities of Daily Living Scale; SF-36, Short Form–36.
[b]Comparison between pre- and postoperative scores.

survivorship analysis and the inclusion of patients treated with synthetic scaffolds, which have since been reported to have high failure rates.[8] Frank et al[9] reported on 180 patients who were treated with OCA and had a mean follow-up of 5 years. More than half (52%) underwent a concomitant procedure, including 65 (36%) who received a concomitant meniscus allograft transplantation. The authors found no correlation between age and failure rate. Two older studies each reported on >122 patients treated with OCA who had a mean follow-up of 7 to 10 years.[11,23] Both studies found an increased risk of failure among patients aged ≥30 years. However, the majority (82%-100%) of patients in both studies were treated with the shell technique, likely because instrumentation for the press-fit dowel technique was not yet widely used. The shell allograft technique, which depends on screw or pin fixation and a larger surface area of bone-to-bone healing for graft integration, likely has a higher risk of failure in older patients because of their weaker bone and inferior bone-to-bone healing as compared with their younger counterparts.

In our study of patients aged ≥40 years who were treated with OCA via the dowel technique, the failure rate was higher than that reported for younger patients,[9,12,23] which is to be expected, and was comparable to that seen for bipolar OCA.[30] Other studies identified a higher number of previous ipsilateral knee operations as a predictor of failure,[9,23] which held true in our cohort of patients aged ≥40 years. We also identified male sex as a predictor of failure, which is at odds with the results by Hanna et al,[14] who reported higher cartilage loss rates and risk of progression of cartilage defects for women than for men. Of note, sex was not significantly correlated with BMI, pre- or postoperative Marx Activity Rating Scale scores, or OA grade in this study. Degeneration of the knee is often cited as a risk factor for worse outcomes and failure after a cartilage restoration procedure, although rarely is the degree of arthritis stratified and correlated with outcomes. To our knowledge, this study is one of the first to examine the correlation between joint degeneration—as quantified by OA and meniscal volume and quality grades—and the risk of OCA failure. Although worse OA and meniscal volume grades demonstrated a trend toward higher failure rates, neither was a significant predictor of failure in the multivariable model. This may be attributed to the lack of statistical power given the sample size (52 knees) and number of failures (n = 14) observed in this study. Clearly, further work is needed to ascertain the association between preexisting joint degeneration and risk of graft failure, as focal chondral defects, even those small in size, typically coexist with some level of degeneration in the surrounding cartilage. Other factors likely affect graft incorporation and clinical function, such as degree of synovial inflammation and further markers of the “biological milieu” of the joint (expression of inflammatory mediators, matrix metalloproteinases, mediators of apoptosis, etc). Although OCA may be performed in an attempt to delay the disease progression initiated by a cartilage defect, the chronic low-grade joint inflammation that is perpetuated by the surrounding cartilage and synovium is not directly addressed by the surgery. Furthermore, whether a partially resected or poor quality meniscus provides sufficient chondroprotection to a condylar graft has not yet been fully elucidated, as meniscal status is rarely considered a potential contributor to failure in the published literature. Regarding the knees of older patients, where these degenerative processes almost always exist, knowing which radiographic or MRI parameters are indicative of a degenerative cascade that has progressed past the point of being improved by an OCA would help in defining the surgical indications in this older population.

Despite the higher failure rates among patients aged ≥40 years, those with surviving allografts at least 2 years postoperatively reported significant clinical improvement, according to published reports of minimally clinically important differences among patients with knee osteoarthritis.[7,39] The clinically significant improvements in outcome scores across all patients ≥40 years indicate that OCA may be a viable option that delays the eventual need for an arthroplasty for several years while improving quality of life. Although some would argue that OCA should be reserved for younger, active patients owing to the limited availability of grafts, as many as 13% of harvested grafts are currently not utilized within the mandatory time frame.[28] A cost-effectiveness analysis comparing OCA with early arthroplasty is needed to truly assess the utility of OCA as a salvage treatment option for older patients.

Several other limitations of this study deserve mention. Mean follow-up was only 3.6 years, allowing us to make conclusions regarding only the intermediate term after OCA. Longer follow-up is needed to more accurately assess OCA as a salvage treatment for patients aged $\geq$40, as many patients may decide to cope with pain and continue with nonoperative treatments for numerous years before eventually undergoing arthroplasty. Moreover, longer follow-up would allow for the longitudinal tracking of outcome scores to assess for any deterioration in symptoms and function. Six patients experienced failure of their OCA within 2 years of their index procedure. Their outcome scores were not collected and included in the analysis, thus inflating the mean scores reported at final follow-up. Long-leg radiographs to assess preoperative alignment were obtained only for patients with gross deformity. Therefore, some patients may have had subtle malalignment ($<5°$), which could have affected their clinical outcomes after OCA. Medical comorbidities and smoking status, which may affect outcomes after OCA, were not collected. OA scoring for a small subset of knees was performed on MRI or postoperative radiographs. Additionally, analyses of meniscal volume and quality scores were applicable only for patients who received condylar OCA. Patients who were doing poorly may have been more likely to return for care, which would introduce transfer bias and increase reoperation and failure rates. Last, this study consisted of patients who were treated by 2 high-volume surgeons at a single institution, which potentially introduces performance bias.

In conclusion, the treatment of large chondral defects in older patients remains a difficult clinical challenge. In our series of patients aged $\geq$40 years who were treated with OCA, we found a higher failure rate as compared with other studies of younger populations. Specifically, a higher number of previous ipsilateral knee operations, male sex, and higher grades of radiographic osteoarthritis preoperatively were predictors of failure. However, patients with surviving allografts reported clinically significant improvements in outcomes, suggesting that OCA can be valuable as a midterm solution or an effective bridge before the eventual need for arthroplasty. Although OCA can be a good treatment option for select patients within the older population, further work is needed to delineate the association between preexisting joint degeneration and risk of graft failure.

REFERENCES

1. Baltzer AW, Ostapczuk MS, Terheiden HP, Merk HR. Good short- to medium-term results after osteochondral autograft transplantation (OAT) in middle-aged patients with focal, non-traumatic osteochondral lesions of the knee. *Orthop Traumatol Surg Res*. 2016;102(7): 879-884.
2. Barber-Westin SD, Noyes FR, McCloskey JW. Rigorous statistical reliability, validity, and responsiveness testing of the Cincinnati Knee Rating System in 350 subjects with uninjured, injured, or anterior cruciate ligament-reconstructed knees. *Am J Sports Med*. 1999;27(4):402-416.
3. Camp CL, Stuart MJ, Krych AJ. Current concepts of articular cartilage restoration techniques in the knee. *Sports Health*. 2014;6(3): 265-273.
4. Cole BJ, Pascual-Garrido C, Grumet RC. Surgical management of articular cartilage defects in the knee. *J Bone Joint Surg Am*. 2009;91(7):1778-1790.
5. de Windt TS, Bekkers JE, Creemers LB, Dhert WJ, Saris DB. Patient profiling in cartilage regeneration: prognostic factors determining success of treatment for cartilage defects. *Am J Sports Med*. 2009;37(suppl 1):58S-62S.
6. Degen RM, Coleman NW, Chang B, Tetreault D, Mahony GT, Williams RJ. Outcomes following structural grafting of distal femoral osteochondral injuries in patients aged 40 years and older. *J Knee Surg*. 2017;30(3):244-251.
7. Escobar A, Quintana JM, Bilbao A, Arostegui I, Lafuente I, Vidaurreta I. Responsiveness and clinically important differences for the WOMAC and SF-36 after total knee replacement. *Osteoarthritis Cartilage*. 2007;15(3):273-280.
8. Farr J, Gracitelli GC, Shah N, Chang EY, Gomoll AH. High failure rate of a decellularized osteochondral allograft for the treatment of cartilage lesions. *Am J Sports Med*. 2016;44(8):2015-2022.
9. Frank RM, Lee S, Levy D, et al. Osteochondral allograft transplantation of the knee. *Am J Sports Med*. 2017;45(4):864-874.
10. Frank RM, Lee S, Poland SG, Cole BJ. Do outcomes of osteochondral allograft transplantation differ based on age [AOSSM abstract]? *Orthop J Sports Med*. 2017;5(3, suppl 3). doi:10.1177/2325967117S00124.
11. Ghazavi MT, Pritzker KP, Davis AM, Gross AE. Fresh osteochondral allografts for post-traumatic osteochondral defects of the knee. *J Bone Joint Surg Br*. 1997;79(6):1008-1013.
12. Gross AE, Shasha N, Aubin P. Long-term followup of the use of fresh osteochondral allografts for posttraumatic knee defects. *Clin Orthop Relat Res*. 2005;435:79-87.
13. Hambly K, Griva K. IKDC or KOOS? Which measures symptoms and disabilities most important to postoperative articular cartilage repair patients? *Am J Sports Med*. 2008;36(9):1695-1704.
14. Hanna FS, Teichtahl AJ, Wluka AE, et al. Women have increased rates of cartilage loss and progression of cartilage defects at the knee than men: a gender study of adults without clinical knee osteoarthritis. *Menopause*. 2009;16(4):666-670.
15. Irrgang JJ, Anderson AF, Boland AL, et al. Development and validation of the international knee documentation committee subjective knee form. *Am J Sports Med*. 2001;29(5):600-613.
16. Julin J, Jamsen E, Puolakka T, Konttinen YT, Moilanen T. Younger age increases the risk of early prosthesis failure following primary total knee replacement for osteoarthritis: a follow-up study of 32,019 total knee replacements in the Finnish Arthroplasty Register. *Acta Orthop*. 2010;81(4):413-419.
17. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16(4):494-502.
18. Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee: a randomized trial. *J Bone Joint Surg Am*. 2004;86(3):455-464.
19. Kreuz PC, Erggelet C, Steinwachs MR, et al. Is microfracture of chondral defects in the knee associated with different results in patients aged 40 years or younger? *Arthroscopy*. 2006;22(11):1180-1186.
20. Krych AJ, Harnly HW, Rodeo SA, Williams RJ 3rd. Activity levels are higher after osteochondral autograft transfer mosaicplasty than after microfracture for articular cartilage defects of the knee: a retrospective comparative study. *J Bone Joint Surg Am*. 2012;94(11): 971-978.
21. Krych AJ, Robertson CM, Williams RJ 3rd; Cartilage Study Group. Return to athletic activity after osteochondral allograft transplantation in the knee. *Am J Sports Med*. 2012;40(5):1053-1059.

22. Lee GW, Son JH, Kim JD, Jung GH. Is platelet-rich plasma able to enhance the results of arthroscopic microfracture in early osteoarthritis and cartilage lesion over 40 years of age? *Eur J Orthop Surg Traumatol*. 2013;23(5):581-587.
23. Levy YD, Gortz S, Pulido PA, McCauley JC, Bugbee WD. Do fresh osteochondral allografts successfully treat femoral condyle lesions? *Clin Orthop Relat Res*. 2013;471(1):231-237.
24. Marcacci M, Kon E, Zaffagnini S, et al. Multiple osteochondral arthroscopic grafting (mosaicplasty) for cartilage defects of the knee: prospective study results at 2-year follow-up. *Arthroscopy*. 2005;21(4):462-470.
25. Marx RG, Jones EC, Allen AA, et al. Reliability, validity, and responsiveness of four knee outcome scales for athletic patients. *J Bone Joint Surg Am*. 2001;83(10):1459-1469.
26. Marx RG, Stump TJ, Jones EC, Wickiewicz TL, Warren RF. Development and evaluation of an activity rating scale for disorders of the knee. *Am J Sports Med*. 2001;29(2):213-218.
27. McAllister DR, Joyce MJ, Mann BJ, Vangsness CT Jr. Allograft update: the current status of tissue regulation, procurement, processing, and sterilization. *Am J Sports Med*. 2007;35(12):2148-2158.
28. McCulloch PC, Gortz S. Osteochondral allograft transplantation: the rationale and basic science. In: Emans P, Peterson L, eds. *Developing Insights in Cartilage Repair*. London, England: Springer-Verlag; 2014:131-147.
29. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care*. 1993;31(3):247-263.
30. Meric G, Gracitelli GC, Gortz S, De Young AJ, Bugbee WD. Fresh osteochondral allograft transplantation for bipolar reciprocal osteochondral lesions of the knee. *Am J Sports Med*. 2015;43(3):709-714.
31. Mithoefer K, Williams RJ 3rd, Warren RF, Wickiewicz TL, Marx RG. High-impact athletics after knee articular cartilage repair: a prospective evaluation of the microfracture technique. *Am J Sports Med*. 2006;34(9):1413-1418.
32. Niemeyer P, Kostler W, Salzmann GM, Lenz P, Kreuz PC, Sudkamp NP. Autologous chondrocyte implantation for treatment of focal cartilage defects in patients age 40 years and older: a matched-pair analysis with 2-year follow-up. *Am J Sports Med*. 2010;38(12):2410-2416.
33. Rand JA, Ilstrup DM. Survivorship analysis of total knee arthroplasty: cumulative rates of survival of 9200 total knee arthroplasties. *J Bone Joint Surg Am*. 1991;73(3):397-409.
34. Rosenberger RE, Gomoll AH, Bryant T, Minas T. Repair of large chondral defects of the knee with autologous chondrocyte implantation in patients 45 years or older. *Am J Sports Med*. 2008;36(12):2336-2344.
35. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee: average 11-year follow-up. *Arthroscopy*. 2003;19(5):477-484.
36. Steadman JR, Miller BS, Karas SG, Schlegel TF, Briggs KK, Hawkins RJ. The microfracture technique in the treatment of full-thickness chondral lesions of the knee in National Football League players. *J Knee Surg*. 2003;16(2):83-86.
37. Veith FU, Menetrey J. Surgical treatment of cartilage tear: principles and results. In: Bonnin M, Amendola A, Bellemans J, MacDonald SJ, Menetrey J, eds. *The Knee Joint: Surgical Techniques and Strategies*. Paris, France: Springer-Verlag France; 2012:457-483.
38. Williams RJ 3rd, Ranawat AS, Potter HG, Carter T, Warren RF. Fresh stored allografts for the treatment of osteochondral defects of the knee. *J Bone Joint Surg Am*. 2007;89(4):718-726.
39. Williams VJ, Piva SR, Irrgang JJ, Crossley C, Fitzgerald GK. Comparison of reliability and responsiveness of patient-reported clinical outcome measures in knee osteoarthritis rehabilitation. *J Orthop Sports Phys Ther*. 2012;42(8):716-723.