Osteochondral Allograft Transplantation of the Knee

Analysis of Failures at 5 Years

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Background: Osteochondral allograft transplantation (OAT) is being performed with increasing frequency, and the need for reoperations is not uncommon.

Purpose: To quantify survival for OAT and report findings at reoperations.

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

Methods: A review of prospectively collected data of 224 consecutive patients who underwent OAT by a single surgeon with a minimum follow-up of 2 years was conducted. The reoperation rate, timing of reoperation, procedure performed, and findings at surgery were reviewed. Failure was defined by revision OAT, conversion to knee arthroplasty, or gross appearance of graft failure at second-look arthroscopic surgery.

Results: A total of 180 patients (mean [±SD] age, 32.7 ± 10.4 years; 52% male) who underwent OAT with a mean follow-up of 5.0 ± 2.7 years met the inclusion criteria (80% follow-up). Of these, 172 patients (96%) underwent a mean of 2.5 ± 1.7 prior surgical procedures on the ipsilateral knee before OAT. Forty-eight percent of OAT procedures were isolated, while 52% were performed with concomitant procedures including meniscus allograft transplantation (MAT) in 65 (36%). Sixty-six patients (37%) underwent a reoperation at a mean of 2.5 ± 2.5 years, with 32% (21/66) undergoing additional reoperations (range, 1-3). Arthroscopic debridement was performed in 91% of patients with initial reoperations, with 83% showing evidence of an intact graft; of these, 9 ultimately progressed to failure at a mean of 4.1 ± 1.9 years. A total of 24 patients (13%) were considered failures at a mean of 3.6 ± 2.6 years after the index OAT procedure because of revision OAT (n = 7), conversion to arthroplasty (n = 12), or appearance of a poorly incorporated allograft at arthroscopic surgery (n = 5). The number of previous surgical procedures was independently predictive of reoperations and failure; body mass index was independently predictive of failure. Excluding the failed patients, statistically and clinically significant improvements were found in the Lysholm score, International Knee Documentation Committee score, Knee injury and Osteoarthritis Outcome Score, and Short Form–12 physical component summary at final follow-up ($P <$ .001 for all), with inferior outcomes (albeit overall improved) in patients who underwent a reoperation.

Conclusion: In this series, there was a 37% reoperation rate and an 87% allograft survival rate at a mean of 5 years after OAT. The number of previous ipsilateral knee surgical procedures was predictive of reoperations and failure. Of the patients who underwent arthroscopic debridement with an intact graft at the time of arthroscopic surgery, 82% experienced significantly improved outcomes, while 18% ultimately progressed to failure. This information can be used to counsel patients on the implications of a reoperation after OAT.

Keywords: cartilage restoration; meniscus transplantation; clinical outcomes; prior arthroscopic surgery; knee arthroplasty

Symptomatic, full-thickness articular cartilage defects in the knee are difficult to manage, especially in the young, high-demand patient population. A variety of cartilage repair and restoration procedures are available, with encouraging short- and long-term clinical outcomes.[2,3,12,14,29,35,41] Recently, several authors have begun to describe symptomatic lesions not only as the result of the articular cartilage defect but also because of the effect of the injury on the underlying subchondral bone.[10,46] As such, certain articular cartilage repair strategies, including microfracture and cell-based therapies, may not be adequate to address the lesion's bony involvement, which may be equally, if not more, responsible for symptom generation when compared with the actual articular defect. Reconstruction techniques, including osteochondral autograft transplantation as well as osteochondral

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allograft transplantation (OAT), are surgical solutions that address both the cartilage and the osseous components of the injury. The autograft option is attractive in that it is a single-stage procedure that involves the harvest of osteoarticular plugs from a nonarticulating portion of the knee, followed by the placement of these plugs into the defect site; no foreign tissue is required. Given the need to use the healthy osteoarticular plugs from the patient, this technique may be best suited for smaller (<2 cm^2) lesions, and certainly, there is some concern over donor-site morbidity.[36,37,40] With advances in surgical instrumentation and expanding indications, OAT is being performed with increasing frequency. The benefits of OAT are many, including the ability to treat larger defects, lack of donor-site morbidity and reduced surgical time, and ability to customize the graft to the recipient's defect site. Further, many authors have reported good to excellent clinical outcomes after primary OAT, after OAT as a salvage procedure for failed prior cartilage restoration, and after OAT combined with meniscus allograft transplantation (MAT).[‡]

However, some concerns over OAT remain, including cost concerns, unavailability of allograft tissue, and disease transmission.[14,44] The overall complication rate after OAT is low; however, one of the more poorly understood complications after OAT is the need for reoperations. The term "reoperation" is used to describe any return trip to the operating room for a procedure on the ipsilateral knee, at any point, after OAT. As such, reoperations after OAT (in association with any concomitant procedure performed at the time of OAT) are extremely variable, ranging from arthroscopic debridement to total knee arthroplasty (TKA), and are not necessarily synonymous with OAT failure.

In a recent assessment of the senior author's (B.J.C.) database of MAT,[30] the authors found a relatively high reoperation rate of 32% in the first 5 years after MAT but an overall allograft survival rate of 95%. These data indicate that despite the relatively high reoperation rate, given the 95% allograft survival rate, a reoperation itself is not necessarily indicative of failure. Importantly, the authors did observe that a reoperation within the first 2 years after MAT is associated with an increased likelihood of revision MAT or future knee arthroplasty, surgical procedures consistent with the failure of the index MAT procedure.[30] Thus, given the association between early reoperations after meniscus restoration surgery and subsequent failure, an improved understanding of the epidemiology and implications of reoperations after OAT (with and without concomitant procedures) is warranted.

Therefore, the purpose of this study was to quantify survival for OAT and report findings at reoperations. We hypothesized that a reoperation within the first 2 years after OAT (with and without concomitant procedures) would be associated with a poor outcome and that concomitant OAT with MAT would be associated with a poor outcome.

METHODS

A total of 224 consecutive patients undergoing OAT by a single surgeon over an 11-year period between 2003 and 2014 were identified from a prospectively collected database. Inclusion criteria included patients undergoing primary OAT by the senior surgeon within a minimum clinical follow-up of 2 years. Patients were included if they had undergone prior ipsilateral knee surgery (other than prior OAT) or if they underwent concomitant procedures at the time of OAT (including, but not limited to, MAT, ligament reconstruction, and/or corrective realignment procedures such as high tibial osteotomy [HTO] or distal femoral osteotomy [DFO]). Patients younger than 15 years were excluded. Demographic, preoperative, intraoperative, and postoperative data were collected for all patients. Demographic data included age, sex, body mass index (BMI), and insurance status (including workers' compensation status). Preoperative data included the mechanism of injury, type of athlete, and number and type of prior ipsilateral knee surgical procedures. Intraoperative data included laterality, compartment, size of the defect relative to size of the involved condyle, depth of the defect, and concomitant procedures performed. Postoperative data included complications, reoperations, and clinical outcome scores at a minimum of 2 years after surgery. Preoperative and postoperative (minimum 2 years after surgery) validated clinical outcome scores were collected and analyzed, including the Lysholm score, International Knee Documentation Committee (IKDC) score, Knee injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form–12 mental component summary (SF-12 MCS) and physical component summary (SF-12 PCS).

Concomitant procedures at the time of OAT were classified as (1) OAT with MAT, (2) OAT with a realignment procedure (HTO or DFO), (3) OAT with anterior cruciate ligament (ACL) reconstruction, and (4) OAT ± MAT ± osteotomy ± ACL reconstruction. The reoperation rate,

‡References 1, 3, 4, 6, 7, 9, 11, 17-19, 22-24, 26, 32, 33, 42, 43.

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timing of reoperation, procedure performed, and findings at the time of reoperation were reviewed. The indications for a reoperation were persistent or recurrent knee pain, mechanical symptoms, or disabling swelling that were typically unresponsive to nonsurgical care including reassurance, activity modification, physical therapy, and injection therapy. Considerations for surgery included frank discussions related to the likelihood of successful reduction in the patient's unacceptable symptoms based on their subjective complaints, physical examination findings, and radiographic assessment results. A reoperation was defined as any subsequent surgical procedure on the ipsilateral knee, including surgical debridement, chondroplasty, second-look arthroscopic surgery, hardware removal, revision OAT, or knee arthroplasty. Failure was defined by revision OAT, conversion to knee arthroplasty, or gross appearance of graft failure at second-look arthroscopic surgery.

Surgical Technique

The surgical technique for OAT has been previously described (Figure 1).[31] In brief, after an examination under anesthesia, diagnostic arthroscopic surgery is performed with visual confirmation of the suspected lesion, ligament reconstruction (if indicated), MAT (if indicated), mini-arthrotomy and OAT, osteotomy (if indicated), and wound closure. After arthroscopic surgery and any concomitant procedures as described above, mini-arthrotomy is performed via a parapatellar incision on the side of the patellar tendon of the involved compartment. The patella is retracted with a Z retractor or bent Hohmann retractor. The defect site is identified, and preparation of the defect bed is begun. At any time after the defect site is confirmed, the allograft can be slowly thawed on the back table. A cannulated, cylindrical sizing guide (Arthrex Inc) is placed flush on the defect to determine the optimal allograft plug diameter, and a guide pin is driven through the guide into the base of the defect. The sizing guide is removed and taken to the back table to be used to help size the donor plug. A cannulated bone reamer is then placed over the guide wire, and the defect is reamed to a depth of approximately 6 to 8 mm. A ruler is used to measure the depth of the defect socket at the 3-, 6-, 9-, and 12-o'clock positions. On the back table, the donor condyle is sized using the previously selected cylindrical sizing guide, and the 12-o'clock position is marked. A donor harvester is passed through the housing and advanced through the entire depth of the donor graft. The plug is then extracted from the harvester. An assistant secures the plug with a forceps, taking care to avoid damage to the articular surface, and a sagittal saw is then used to finalize the depth of the plug according to the previously measured defect depths at 3, 6, 9, and 12 o'clock. Pulsatile lavage is used on the allograft plug to remove any remaining marrow elements. At this time, the graft is carefully brought to the surgical field, and the 12-o'clock position on the plug is aligned with the 12-o'clock position on the defect, and the graft is pressed into place by hand. If needed, an oversized tamp can be used to gently affect the graft into the defect bed to ensure

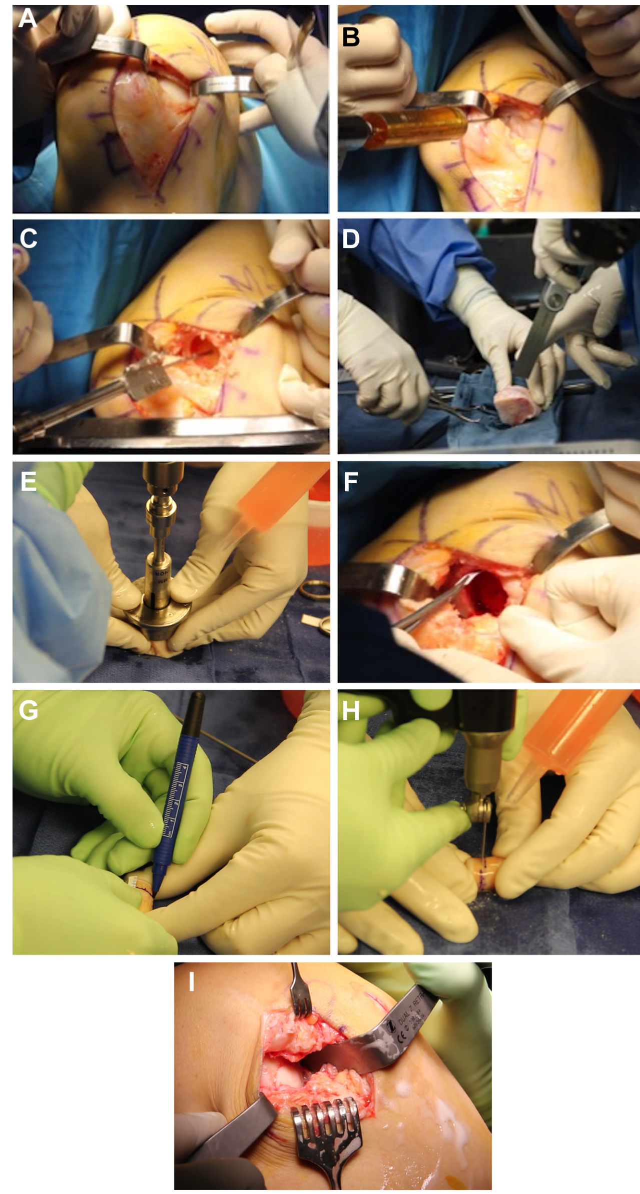

Figure 1. Intraoperative photographs of a 28-year-old man undergoing right knee medial opening wedge high tibial osteotomy with concomitant medial femoral condyle (MFC) osteochondral allograft transplantation. Shown here are several aspects of the osteochondral allograft portion of the procedure: (A) medial arthrotomy to gain exposure to the MFC, (B) identification of a full-thickness defect of the MFC, (C) preparation of the defect bed before measurement and transplantation of the prepared allograft, (D) allograft harvest from a fresh femoral hemicondyle, (E) sizing of the allograft with a circular saw, (F) measurement of the defect depth with a ruler, (G) measurement of the allograft plug with a ruler to confirm the appropriate depth before cutting, (H) creating an appropriately sized allograft with a sagittal saw, and (I) final allograft placement into the MFC.

a secure press fit; care should be taken to minimize the force and number of impactions to preserve chondrocyte viability.[27,39] If additional fixation is needed, compression screws (Arthrex Inc) can be used. The wound is irrigated and closed in layers in a standard fashion.

Rehabilitation Protocol

The postoperative rehabilitation protocol consisted of a 4- to 6-week period of protected weightbearing in a hinged knee brace, followed by progression to full weightbearing as tolerated.[31] During this initial period, patients were permitted to begin range of motion exercises, quadriceps sets, straight-leg raises, and patellar mobilization. A stationary bicycle was permitted at 4 weeks, and the brace was discontinued between weeks 4 and 8, pending the patient's quadriceps strength. No open chain exercises were permitted in this first phase. Early weightbearing range of motion (0°-90°) was restricted until 4 to 6 weeks after surgery. Gentle strengthening was begun at the 6-week point and was increased with gentle recreational exercises over the next 2 to 3 months. Patients progressed to sport-specific activities by 4 to 6 months after surgery for isolated OAT and by 8 to 12 months for those undergoing concomitant procedures.

Statistical Analysis

Statistical analysis was performed utilizing descriptive statistics, chi-square testing, independent-samples *t* tests, multivariate analysis of variance, and bivariate logistic regression analysis. The bivariate logistic regression model included sex, age, BMI, workers' compensation status, number of previous ipsilateral knee surgical procedures, major concomitant knee surgery at the time of OAT, concomitant MAT, number of osteochondral allograft lesions, and ratio of defect size to femoral condyle area. In addition, Kaplan-Meier survival analysis was performed with survival defined as the absence of revision OAT or knee arthroplasty. The analysis assumed a nonparametric distribution of time-dependent survival, similar behavior between procedures that were performed at different time periods, and similar survival behavior between censored (those not yet meeting the endpoint of failure) and uncensored (those who met failure criteria) patients. A comparison of survival between medial, lateral, and multisite OAT was conducted via the log-rank test. Odds ratios (ORs) were obtained using cross-tabulation, and a 2-tailed Fisher exact probability test was performed to assess statistical significance. All reported *P* values are 2-tailed, with an α level of .05 detecting significant differences (SPSS Statistics version 23.0; IBM Corp).

RESULTS

Of 224 patients, 180 (mean age, 32.7 ± 10.4 years; 93 male, 87 female) who underwent OAT with a mean follow-up of 5.0 ± 2.7 years (range, 2.0-15.1 years) were included (80% follow-up) (Table 1). Of these, 172 patients (96%) underwent a mean of 2.5 ± 1.7 prior surgical procedures on the ipsilateral knee before OAT. Forty-eight percent of OAT procedures were isolated, while 52% were performed with concomitant procedures including MAT in 65 (36%) (Table 2). The duration of symptoms before OAT was available for 112 of the 180 patients (62%) and was found to be a mean of 4.0 ± 4.8 years.

Reoperations

A total of 66 patients (37%) underwent a reoperation at a mean of 2.5 ± 2.5 years, with 32% of these patients (21/66) undergoing additional reoperations (range, 1-3 additional reoperations); 59% (39/66) underwent reoperations that were performed within 2 years of the index OAT procedure (Tables 1 and 3). Indications for a reoperation included persistent effusion, pain, mechanical symptoms, and/or stiffness after OAT, appropriate rehabilitation, and nonoperative treatment modalities. Patients indicated for a reoperation underwent preoperative magnetic resonance imaging in an effort to better identify the symptomatic pathological disorders, although in many cases, the imaging findings were limited by postoperative changes. Arthroscopic debridement was performed in 91% (60/66) of patients with initial reoperations, with 50 (83%) showing arthroscopic evidence of an intact graft; of these 50 patients, 9 ultimately progressed to failure at a mean of 4.1 ± 1.9 years.

Failures and Complications

A total of 24 patients (13%) were considered failures at a mean of 3.6 ± 2.6 years after the index OAT procedure because of revision OAT (n = 7), conversion to arthroplasty (n = 12), or appearance of a poorly incorporated allograft at arthroscopic surgery (n = 5). There were a total of 10 complications (3.33%), for which 4 patients required surgery (2 for arthrofibrosis, 1 for hematoma, and 1 for deep infection) (Table 4).

Analysis of Risk Factors for Reoperation and Failure

Patients requiring a reoperation had a significantly greater number of previous ipsilateral knee surgical procedures (2.97 ± 1.59 vs 2.19 ± 1.66, respectively; *P* = .002) and a higher proportion of workers' compensation claims (29% vs 16%, respectively; *P* = .038) compared with patients not requiring reoperations. Patients who required a reoperation and were considered failures had a significantly higher BMI (29.42 ± 5.29 vs 26.27 ± 4.96 kg/m^2, respectively; *P* = .017) as well as a significantly greater number of previous ipsilateral knee surgical procedure (3.75 ± 1.89 vs 2.52 ± 1.19, respectively; *P* = .002) as compared with patients who required a reoperation but were not considered a failure. Patients who were considered a failure in the cohort in general (with or without reoperations) had a significantly higher BMI (29.42 ± 5.29 vs 26.00 ± 4.96 kg/m^2, respectively; *P* = .003) and a significantly greater number of previous ipsilateral knee surgical procedures (3.75 ± 1.89 vs 2.28

TABLE 1
Patient Demographics and Results of Procedures[a]

	All Patients (N = 180)	No Reoperations (n = 114)	All Reoperations After OAT (n = 66)	Reoperations After OAT, Nonfailures (n = 42)	Reoperations After OAT, Failures (n = 24)
Age, y	32.74 ± 10.40	31.97 ± 10.97	34.07 ± 9.27	33.30 ± 9.49	35.42 ± 8.91
Body mass index, kg/m^2	26.47 ± 5.12	25.90 ± 5.10	27.44 ± 5.06	26.27 ± 4.59	29.42 ± 5.29
Side (left/right), n	87/93	53/61	34/32	20/22	14/10
Sex (female/male), n	87/93	59/55	28/38	20/22	8/16
Athlete (no/yes), n	120/60	67/47	49/17	20/22	20/4
Workers' compensation (no/yes), n	143/37	94/20	46/20	29/13	16/8
Follow-up, y	4.98 ± 2.65	4.63 ± 2.33	5.28 ± 3.27	5.52 ± 2.96	4.86 ± 3.78
No. of previous surgeries	2.48 ± 1.67	2.19 ± 1.66	2.97 ± 1.59	2.52 ± 1.19	3.75 ± 1.89
No. of OA sites	1.10 ± 0.37	1.10 ± 0.40	1.11 ± 0.31	1.20 ± 0.30	1.13 ± 0.34
Largest OA defect area, mm^2	352.36 ± 152.21	342.20 ± 144.17	369.99 ± 164.93	343.54 ± 130.69	414.08 ± 205.68
Defect:condyle ratio	0.17 ± 0.11	0.16 ± 0.10	0.18 ± 0.11	0.17 ± 0.09	0.20 ± 0.15
OAT location, n					
LFC	73	50	23	16	7
MFC	116	69	47	28	19
Trochlea	6	3	2	1	2
Patella	2	2	1	1	0
Major concomitant surgery (no/yes), n	87/93	55/59	32/34	23/19	9/15
Any MAT (no/yes), n	115/65	72/42	43/23	28/14	15/9
Medial MAT (no/yes), n	144/36	92/22	52/14	34/8	18/6
Lateral MAT (no/yes), n	150/30	93/21	57/9	36/6	21/3
No. of reoperations	N/A	N/A	1.30 ± 0.61	1.12 ± 0.33	1.63 ± 0.82
Time to first reoperation, y	N/A	N/A	2.51 ± 2.51	2.44 ± 2.60	2.64 ± 2.41

[a]Data are reported as mean ± SD unless otherwise indicated. LFC, lateral femoral condyle; MAT, meniscus allograft transplantation; MFC, medial femoral condyle; N/A, not applicable; OA, osteochondral allograft; OAT, osteochondral allograft transplantation.

TABLE 2
Description of Concomitant Procedures[a]

Major Concomitant Procedure	No. of Patients
Ligament repair/reconstruction	3 (1 PCL, 1 revision ACL, 1 ACL)
MAT	65 (29 lateral, 35 medial, 1 lateral and medial)
HTO	15
Distal femoral osteotomy	9
Anteromedialization	4
Microfracture to area other than OAT site	9
Partial meniscectomy	4

[a]52% of the population underwent at least 1 concomitant procedure at the time of OAT, with some patients undergoing more than 1 concomitant procedure (ie, OAT with MAT with HTO). ACL, anterior cruciate ligament; HTO, high tibial osteotomy; MAT, meniscus allograft transplantation; OAT, osteochondral allograft transplantation; PCL, posterior cruciate ligament.

± 1.55, respectively; $P < .0001$) as compared with nonfailures.

Logistic Regression

Using a logistic regression model including sex, age, BMI, workers' compensation status, number of previous ipsilateral knee surgical procedures, major concomitant knee surgery at the time of OAT (including concomitant MAT), number of osteochondral allograft lesions, ratio of defect to condyle size, and history of microfracture, the number of previous surgical procedures was independently predictive of reoperations (OR, 1.46 [95% CI, 1.141-1.869]; $P = .003$). If a patient underwent a reoperation, the number of previous surgical procedures (OR, 2.988 [95% CI, 1.364-6.544]; $P = .006$) and BMI (OR, 1.297 [95% CI, 1.052-1.600]; $P = .15$) were predictive of failure. Overall, BMI was predictive of failure for those who underwent reoperations as well as failures in the context of the entire cohort in general but was not an independent predictor of reoperations.

When the cohort was taken as a whole regardless of reoperations, the number of previous surgical procedures (OR, 1.76 [95% CI, 1.244-2.476]; $P = .001$) and BMI (OR, 1.165 [95% CI, 1.035-1.312]; $P = .12$) were predictive of failure in general. Concomitant MAT was not an independent predictive factor for reoperations ($P = .329$), failure with reoperations ($P = .895$), or failure in general ($P = .506$). Concomitant HTO or DFO (indicating malalignment) was not associated with reoperations or failure ($P > .05$ for all).

Clinical Outcomes

Excluding the failed patients, statistically and clinically significant improvements were found in the Lysholm, Tegner, IKDC, KOOS (all subscales), and SF-12 PCS

TABLE 3
Description of Reoperations[a]

Reoperations	No. of Patients
Initial reoperations[b]	66
Arthroscopic debridement[c]	58
Arthroscopic irrigation and debridement for hematoma	1
Arthroscopic irrigation and debridement for infection	1
Removal of hardware (from DFO)	1
Arthroplasty (total or partial)	5
Additional reoperations[d]	21
Arthroscopic debridement	8
Subsequent arthroplasty after arthroscopic surgery	3
Arthroscopic debridement with revision MAT	1
Arthroscopic debridement with revision MAT and revision ACL reconstruction	1
Revision OAT (3 with concomitant MAT, 1 with concomitant DFO)	7
Arthroplasty (total or partial)	4

[a]ACL, anterior cruciate ligament; DFO, distal femoral osteotomy; MAT, meniscus allograft transplantation; OAT, osteochondral allograft transplantation.
[b]A total of 66 patients (37% of cohort) underwent a reoperation.
[c]Arthroscopic surgery was performed in 91% (60/66) of patients with initial reoperations, with 50 (83%) showing arthroscopic evidence of an intact graft; of these, 9 ultimately progressed to failure at a mean of 4.1 ± 1.9 years.
[d]Of 66 patients, 21 underwent additional reoperations (range, 1-3 additional reoperations).

TABLE 4
Description of Complications

Complication	No. of Patients
Arthrofibrosis requiring arthroscopic lysis of adhesions	2
Superficial wound infection not requiring surgery	2
Peroneal nerve palsy (transient)	1
Venous thromboembolism	1
Traumatic fall prompting second-look arthroscopic surgery	1
Complex regional pain syndrome	1
Deep infection requiring arthroscopic irrigation	1
Acute hematoma requiring arthroscopic irrigation	1

($P < .001$ for all) outcome assessments at final follow-up (Figure 2). Specifically, there were improvements in the mean Lysholm score (41.5 ± 16.2 to 63.5 ± 22.6), Tegner score (2.90 ± 1.75 to 6.28 ± 2.65), IKDC score (33.8 ± 13.7 to 59.2 ± 21.4), KOOS-Pain (53.9 ± 16.9 to 74.4 ± 19.0), KOOS-Symptoms (55.6 ± 16.4 to 72.3 ± 18.2), KOOS–Activities of Daily Living (KOOS-ADL; 63.9 ± 21.7 to 84.0 ± 18.5), KOOS-Sport (24.3 ± 20.1 to 50.4 ± 26.9), KOOS–Quality of Life (KOOS-QoL; 23.6 ± 18.9 to 51.5 ± 25.1), and SF-12 PCS (35.5 ± 6.85 to 43.5 ± 7.36).

Comparatively inferior outcomes (albeit still significantly improved compared with preoperative scores) were found in patients who underwent reoperations in the Tegner score, IKDC score, KOOS-Pain, KOOS-ADL, KOOS-Sport, KOOS-QoL, and SF-12 PCS ($P < .05$ for all). Specifically, in the reoperation cohort, there were improvements in the mean Tegner score (2.48 ± 1.53 to 5.02 ± 2.85), IKDC score (32.3 ± 13.8 to 48.4 ± 21.8), KOOS-Pain (54.2 ± 14.9 to 65.1 ± 19.8), KOOS-ADL (63.7 ± 18.9 to 76.6 ± 20.4), KOOS-Sport (25.3 ± 21.7 to 41.0 ± 24.2), KOOS-QoL (23.1 ± 21.7 to 39.7 ± 26.5), and SF-12 PCS (36.2 ± 5.70 to 41.4 ± 7.82).

Patients who underwent reoperations had significantly lower Lysholm, Tegner, IKDC, and KOOS (all subscale) scores at final follow-up ($P < .05$ for all). Specifically, in the reoperation cohort, there were superior mean values in the Lysholm score (67.8 ± 20.5 vs 51.8 ± 24.0, respectively), Tegner score (6.75 ± 2.43 vs 5.02 ± 2.85, respectively), IKDC score (63.1 ± 19.8 vs 48.4 ± 21.8, respectively), KOOS-Pain (77.9 ± 17.5 vs 65.1 ± 19.8, respectively), KOOS-Symptoms (75.0 ± 17.3 vs 65.0 ± 18.7, respectively), KOOS-ADL (86.7 ± 17.1 vs 76.6 ± 20.4, respectively), KOOS-Sport (53.8 ± 27.1 vs 41.0 ± 24.2, respectively), and KOOS-QoL (55.8 ± 23.2 vs 39.7 ± 26.5, respectively) compared with those who did not require reoperations. There were no significant differences in the SF-12 PCS or MCS between patients who underwent reoperations and those who did not at final follow-up ($P > .05$).

Medial Versus Lateral Femoral Condyle Grafts

Kaplan-Meier survival analysis was performed to assess for differences in survival based on compartment. While medial femoral condyle (MFC) grafts demonstrated the highest mean survival time (4.279 years), followed by multisite grafts (2.650 years) and lateral femoral condyle (LFC) grafts (2.187 years), these results were not statistically significant ($P = .475$) (Figure 3).

Influence of Concomitant MAT

Kaplan-Meier survival analysis was also performed for concomitant MAT (Figure 4), with the log-rank test demonstrating no significant difference in survival distributions between patients with and without concomitant MAT ($P = .899$).

Influence of History of Microfracture

Kaplan-Meier survival analysis was also performed for previously failed microfracture (Figure 5), with the log-rank test demonstrating no significant difference in survival distributions of OAT between patients with and without a history of microfracture ($P = .370$).

Overall, based on the survivorship analyses, patient history of failed microfracture did not significantly affect graft survivorship, concomitant MAT did not significantly affect graft survivorship, and graft compartment (MFC vs LFC vs multisite) did not significantly affect graft survivorship.

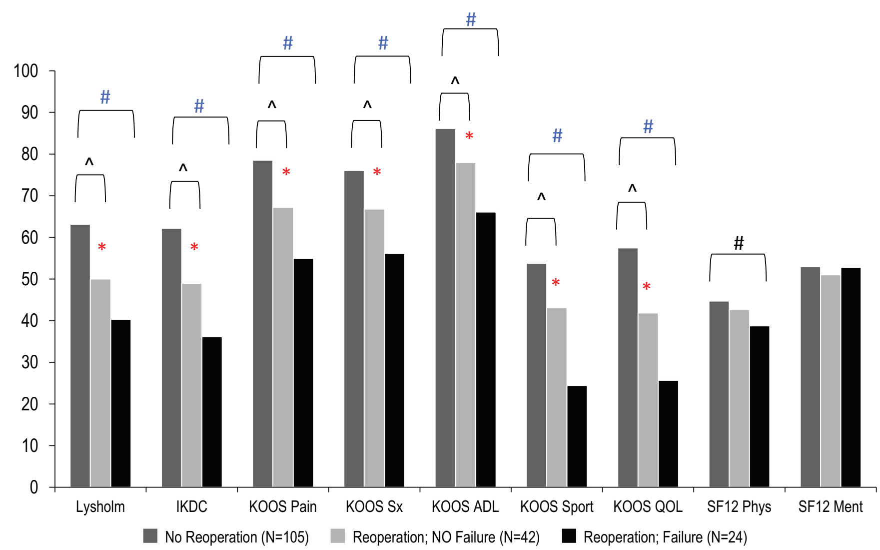

Figure 2. Multivariate analysis of postoperative outcomes at a mean of 5.0 ± 2.7 years. Patients with no reoperations or failures had significantly higher Lysholm scores, International Knee Documentation Committee (IKDC) scores, and Knee injury and Osteoarthritis Outcome Score (KOOS) values compared with patients with reoperations without failures (^) in addition to significantly higher Lysholm scores, IKDC scores, KOOS values, and Short Form–12 physical component summary (SF-12 PCS) scores compared with patients who failed (#). Patients who underwent reoperations without failure demonstrated significantly higher Lysholm scores, IKDC scores, and KOOS values compared with failures (*).

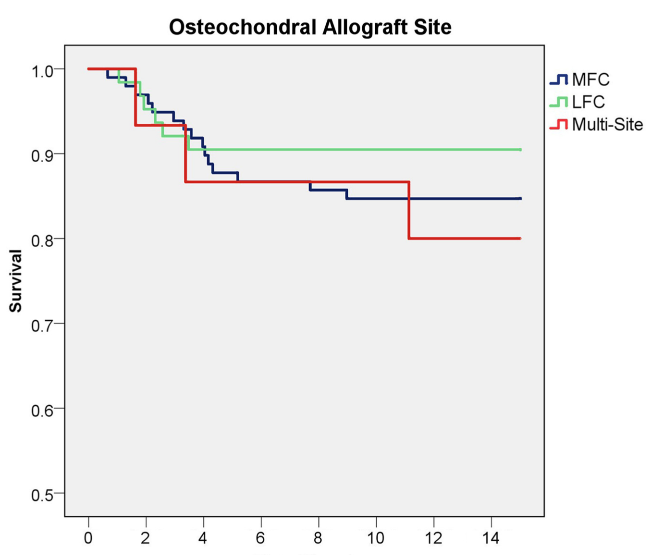

Figure 3. Kaplan-Meier survival analysis was performed, with medial femoral condyle (MFC) grafts demonstrating the highest survival time (4.279 years), followed by multisite grafts (2.650 years) and lateral femoral condyle (LFC) grafts (2.187 years). Respective survival probabilities at 1, 2, 3, 5, and 10 years were 100%, 95.2%, 92.1%, 90.5%, and 90.5% for MFC grafts; 99%, 96.7%, 93.9%, 87.8%, and 84.7% for LFC grafts; and 100%, 93.3%, 93.3%, 86.7%, and 86.7% for multisite grafts. The log-rank test demonstrated a significant difference in survival distributions between these groups (*P* = .475).

DISCUSSION

The principal findings of this study demonstrate that (1) there is an overall 37% reoperation rate with an 87% allograft survival rate at 5 years after OAT (with or without concomitant procedures); (2) arthroscopic debridement is the most common reoperation procedure performed after OAT (with and without concomitant procedures), accounting for 91% of reoperations; (3) the number of previous ipsilateral knee surgical procedures as well as BMI are independent factors predictive of reoperations and failure after the index OAT procedure; and (4) of the patients who underwent arthroscopic debridement with an intact graft at the time of arthroscopic surgery, 82% experienced significantly improved outcomes, while 18% ultimately progressed to failure.

The authors hypothesized that reoperations within the first 2 years after OAT would be associated with poor outcomes and that concomitant OAT with MAT would be associated with a poor outcome. We were unable to prove either of these hypotheses based on the data collected in the study. First, because of the number of reoperations considered failures (3 revision OAT, 2 arthroplasty, and 2 appearance of graft failure) accounting for the primary reoperation within the first 2 years after OAT, we were unable to determine if a reoperation within 2 years was a predictor of failure, as the variable of reoperation itself becomes a confounding factor when analyzing all variables statistically. Second, and surprisingly, concomitant OAT with MAT was not an independent predictive factor for reoperations (*P* = .836) or failure (*P* = .218). Our hypothesis

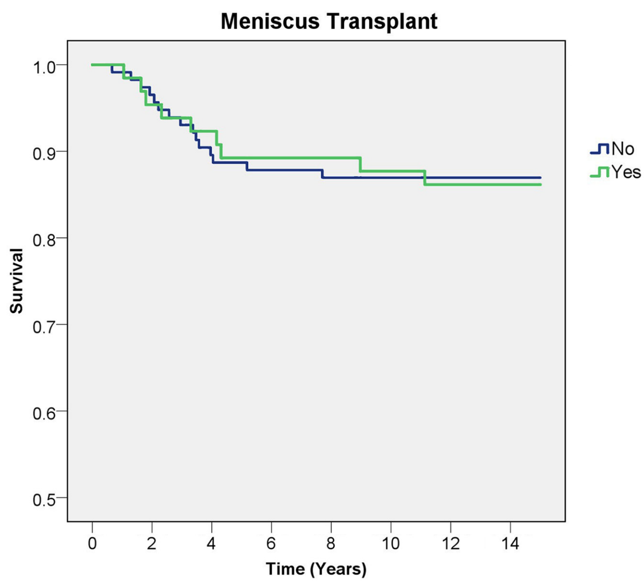

Figure 4. Kaplan-Meier survival analysis for concomitant meniscus allograft transplantation (MAT). Concomitant MAT showed a mean survival of 4.296 years compared with a mean survival of 3.106 years for no concomitant MAT. Respective survival probabilities at 1, 2, 3, 5, and 10 years were 100%, 95.4%, 93.8%, 89.2%, and 87.7% with concomitant MAT and 99.1%, 96.5%, 93.0%, 88.7%, and 87.0% for no concomitant MAT. The log-rank test showed no significant difference in survival distributions between these groups (*P* = .899).

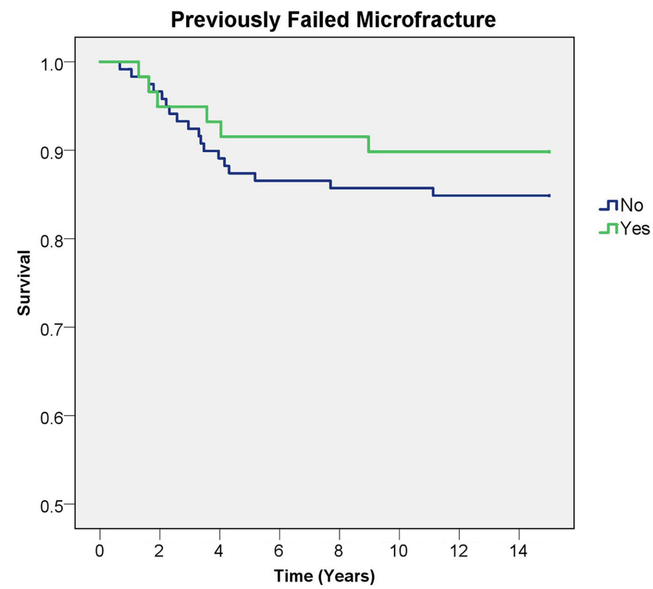

Figure 5. Kaplan-Meier survival analysis for previously failed microfracture. Previously failed microfracture showed a mean survival of 3.570 years compared with the mean survival of no previously failed microfracture of 3.546 years. Respective survival probabilities at 1, 2, 3, 5, and 10 years were 100%, 94.9%, 94.9%, 91.5%, and 89.9% for grafts with previously failed microfracture as compared with 99.2%, 96.6%, 92.4%, 87.4%, and 84.9% for grafts without previously failed microfracture. The log-rank test showed no significant difference in survival distributions between these groups (*P* = .370).

was based on our clinical suspicion that these patients undergo "more surgery" at the time of the index OAT procedure and, thus, at baseline have a worse appearing joint compared with patients not requiring concomitant MAT, which seemingly would result in worse clinical outcomes. As noted above, this was not the case, and thus, patients undergoing concomitant MAT with OAT can be advised that their risk of failure at 5 years after surgery is no different from patients undergoing isolated OAT.

The goal of cartilage restoration surgery is to improve function and reduce pain. The young age and high baseline activity level of the patients included in this study resulted in a significant risk for the development of knee osteoarthritis. Thus, the major indication for surgical intervention in the senior author's patient population is large (>2 cm^2), full-thickness, nonkissing (not bipolar) chondral defects in patients who are symptomatic with chronic pain, mechanical symptoms, recurrent effusions, and/or unacceptable loss of function. Certainly, one of the main questions concerning patients undergoing OAT is the durability of the procedure and its potential to delay and/or avoid the need for future knee surgery, particularly knee arthroplasty. Our study complements previously published studies[20,21] by reporting reoperation rates at medium-term follow-up and further by describing risk factors for failure. The reoperation rate in our cohort of patients is relatively high at 37% at a mean 5-year follow-up, but despite this volume of reoperations, the allograft survival rate is 87% over this same time period. This information is extremely helpful in counseling patients considering OAT, as these patients can be advised of a relatively high chance of allograft survival with excellent clinical outcomes as determined by patient-reported outcome scores at 5 years, provided that concomitant injuries are treated and that surgery was performed for appropriate indications.

On the basis of the results of this study, patients undergoing OAT can be advised of an approximately 1 in 3 chance of undergoing an additional operation on the surgical knee within the first 5 years of OAT. Importantly, over 90% of the reoperations will be associated with substantially less morbidity and a quicker recovery time compared with OAT, as arthroscopic debridement accounted for 91% of reoperations. At the time of arthroscopic debridement, most patients were noted to have mild synovitis, with some patients requiring debridement of the host cartilage edges because of mild degeneration. In other cases, debridement of mild-moderate scar tissue was performed. Patients who choose to undergo OAT are often in a salvage situation, living with debilitating pain and loss of function, with no other joint-preserving option. It is plausible that these patients are likely to accept the risk of reoperations if the overall allograft survival rate is promising.

When comparing our results to other studies, our findings of significantly improved clinical outcome scores in nonfailure patients are consistent with multiple other authors.[4,5,7,13,17,20,21] In 2016, Frank et al[15] reported on reoperation rates after cartilage repair and restoration across a national database of over 50,000 patients. The authors reported an overall reoperation rate of 11.2% after OAT at 2 years, with failures accounting for 12.8% of the reoperations and arthroscopic debridement/chondroplasty/synovectomy accounting for 87.2% of the reoperations. The present results are consistent with the database findings,[15] particularly with respect to the failure rate and procedures performed at the time of reoperation, although the failure rate in the present study is slightly higher (13% at 5 years) compared with the reported 12.8% at 2 years. Notably, the overall absolute postoperative score values were relatively low, especially when compared with other sports medicine procedures about the knee, such as ACL reconstruction or meniscus repair surgery. The magnitude of these scores illustrates the salvage nature of this surgery, particularly in patients with multiple prior ipsilateral knee operations.

In a 2016 systematic review of 20 studies incorporating 1117 patients, Campbell et al[8] assessed return-to-play rates after microfracture, autologous chondrocyte implantation (ACI), osteochondral autograft transfer, and OAT. The authors noted that return-to-sport rates were greatest after osteochondral autograft transfer (89%), followed by OAT (88%), ACI (84%), and microfracture (75%). Positive prognostic factors for return to sport included younger age, shorter duration of preoperative symptoms, no history of ipsilateral knee surgery, and smaller chondral defects. Reoperation rates between the 4 techniques were not statistically compared in their study. In contrast to this systematic review, in the present study, no statistical correlation was found between clinical outcomes or failure rates with age, duration of preoperative symptoms, prior ipsilateral knee surgery, or defect size. As with most systematic reviews assessing the articular cartilage literature, the heterogeneity of studies included in the systematic review, resulting in nonweighted pooling of data, may prohibit the ability to statistically analyze any of these variables in isolation, and thus, a single study within the included 20 studies may have biased the results.

Certainly, a reoperation rate of 37% after an elective knee procedure must be scrutinized carefully, as reoperations, even if minor as was the case in 91% of the reoperations in this cohort, are not without risks. The reoperation rate in this cohort is likely a reflection of the invasiveness of the transplantation procedure itself, in conjunction with the young, demanding, high-level patient population. Reoperation rates[15] after other knee joint preservation procedures are as high as 33% after ACI,[25] 29% after microfracture,[34] 20% after meniscus repair,[38] 32% after MAT,[30] and 27% after ACL reconstruction.[28] While the indications for each of these procedures differ, there are some common findings between them with respect to the technical aspect of the surgical procedure, including subsequent intra-articular bleeding, which may predispose the joint to early scarring, stiffness, and need for early surgical debridement. Importantly, while all nonfailure patients in our cohort, including those undergoing reoperations, experienced statistically and clinically significant improvements in Lysholm, IKDC, KOOS, and SF-12 PCS scores at final follow-up, patients who underwent reoperations had significantly inferior Lysholm, IKDC, KOOS, and SF-12 PCS scores compared with patients who did not undergo reoperations. A variety of factors may account for this finding, including the finding that patients undergoing reoperations had undergone proportionally more previous ipsilateral knee surgical procedures before the index OAT procedure, suggesting that these patients had a "worse" knee at the time of the index OAT procedure.

The 24 patients who failed OAT (13% of the entire cohort), as determined by revision OAT, conversion to arthroplasty, and/or appearance of a failed graft at second-look arthroscopic surgery, represent an extremely challenging patient population. In addition to failing major knee surgery at a relatively young age, the majority of these patients do not perform well after revision surgery, including arthroplasty. Steinhoff and Bugbee[45] analyzed 35 patients undergoing TKA after OAT and found a 31.4% failure rate at 9.2 ± 4.3 years after TKA, with patient age and number of prior surgical procedures associated with an increased risk of failure. Similarly, Frank et al[16] compared the outcomes of 13 patients undergoing arthroplasty after failed prior cartilage restoration to 13 age-, sex-, and BMI-matched controls, and while all patients improved after arthroplasty, there were significantly inferior outcomes in the cartilage restoration group, including a 15% failure rate, compared with the controls (no failures).

Limitations

This study has several limitations. There is a potential for detection bias within the methods. While our follow-up rate of 80% over a course of 11 years in a historically difficult-to-reach, geographically diverse referral patient population is reasonable, the 20% (n = 44) of nonresponding patients may have sought surgical care at another institution without our knowledge, which may bias the results, notably with an underestimation of reoperation and/or failure rates. Patient contact was attempted via multiple modalities at a minimum of 5 times per patient, until they were deemed nonresponding and thus lost to follow-up. Similarly, one factor of interest was the duration of symptoms before OAT, but this was only available for 112 of 180 patients, and thus, this factor was not included in the statistical analyses. There is also a potential for transfer bias, as patients who are doing poorly are more likely to return for care and affect the reoperation rates. There is also a potential for performance bias, as this study was conducted based on the outcomes of a single high-volume surgeon using a single technique. In addition, there is a potential for clinical susceptibility bias, as these patients underwent a joint salvage procedure and likely had a guarded prognosis at baseline. Finally, isolated OAT procedures were performed in 48% of the cohort, with the remainder of patients undergoing concomitant procedures. Thus, the outcomes and reoperation rates presented in this study may have been influenced by the concomitant procedures as opposed to being a reflection of OAT. However, this patient population often presents with multiple coexisting lesions, including irreparable meniscus injuries, malalignment, and/or ligamentous insufficiency, and can require multiple procedures in addition to OAT. Other authors presenting large series of patients undergoing OAT also have substantial populations with concomitant MAT, osteotomy, and ligament reconstruction.

CONCLUSION

To our knowledge, this series represents the single largest series of patients undergoing OAT available in the literature worldwide. In this series, there was a 37% reoperation rate after OAT, of which arthroscopic debridement was the most common (91%), and an 87% allograft survival rate at a mean of 5 years. The number of previous ipsilateral knee surgical procedures was predictive of reoperations and failure. Of the patients who underwent arthroscopic debridement with an intact graft at the time of arthroscopic surgery, 82% experienced significantly improved outcomes, while 18% ultimately progressed to failure. This information can be used to counsel patients on the implications of reoperations after OAT (with and without appropriate concomitant surgery).

REFERENCES

1. Abrams GD, Hussey KE, Harris JD, Cole BJ. Clinical results of combined meniscus and femoral osteochondral allograft transplantation: minimum 2-year follow-up. *Arthroscopy*. 2014;30(8):964-970.e1.
2. Alford JW, Cole BJ. Cartilage restoration, part 1: basic science, historical perspective, patient evaluation, and treatment options. *Am J Sports Med*. 2005;33(2):295-306.
3. Alford JW, Cole BJ. Cartilage restoration, part 2: techniques, outcomes, and future directions. *Am J Sports Med*. 2005;33(3):443-460.
4. Briggs DT, Sadr KN, Pulido PA, Bugbee WD. The use of osteochondral allograft transplantation for primary treatment of cartilage lesions in the knee. *Cartilage*. 2015;6(4):203-207.
5. Bugbee W, Cavallo M, Giannini S. Osteochondral allograft transplantation in the knee. *J Knee Surg*. 2012;25(2):109-116.
6. Bugbee WD, Pallante-Kichura AL, Gortz S, Amiel D, Sah R. Osteochondral allograft transplantation in cartilage repair: graft storage paradigm, translational models, and clinical applications. *J Orthop Res*. 2016;34(1):31-38.
7. Cameron JI, Pulido PA, McCauley JC, Bugbee WD. Osteochondral allograft transplantation of the femoral trochlea. *Am J Sports Med*. 2016;44(3):633-638.
8. Campbell AB, Pineda M, Harris JD, Flanigan DC. Return to sport after articular cartilage repair in athletes' knees: a systematic review. *Arthroscopy*. 2016;32(4):651-668.
9. Chahal J, Gross AE, Gross C, et al. Outcomes of osteochondral allograft transplantation in the knee. *Arthroscopy*. 2013;29(3):575-588.
10. Collins JA, Beutel BG, Strauss E, Youm T, Jazrawi L. Bone marrow edema: chronic bone marrow lesions of the knee and the association with osteoarthritis. *Bull Hosp Jt Dis (2013)*. 2016;74(1):24-36.
11. De Caro F, Bisicchia S, Amendola A, Ding L. Large fresh osteochondral allografts of the knee: a systematic clinical and basic science review of the literature. *Arthroscopy*. 2015;31(4):757-765.
12. Detterline AJ, Goldberg S, Bach BR Jr, Cole BJ. Treatment options for articular cartilage defects of the knee. *Orthop Nurs*. 2005;24(5):361-366, quiz 367-368.
13. Emmerson BC, Görtz S, Jamali AA, Chung C, Amiel D, Bugbee WD. Fresh osteochondral allografting in the treatment of osteochondritis dissecans of the femoral condyle. *Am J Sports Med*. 2007;35(6):907-914.
14. Farr J, Cole B, Dhawan A, Kercher J, Sherman S. Clinical cartilage restoration: evolution and overview. *Clin Orthop Relat Res*. 2011;469(10):2696-2705.
15. Frank RM, McCormick F, Rosas S, et al. Reoperation rates after cartilage restoration procedures in the knee: analysis of a large US commercial database. *Am J Orthop*. In press.
16. Frank RM, Plummer D, Chalmers PN, Cole BJ, Della Valle CJ. Does prior cartilage restoration negatively impact outcomes of knee arthroplasty? *Arthroscopy*. 2015;31(6 Suppl):e23-e24.
17. Getgood A, Gelber J, Gortz S, De Young A, Bugbee W. Combined osteochondral allograft and meniscal allograft transplantation: a survivorship analysis. *Knee Surg Sports Traumatol Arthrosc*. 2015;23(4):946-953.
18. Gracitelli GC, Meric G, Briggs DT, et al. Fresh osteochondral allografts in the knee: comparison of primary transplantation versus transplantation after failure of previous subchondral marrow stimulation. *Am J Sports Med*. 2015;43(4):885-891.
19. Gracitelli GC, Meric G, Pulido PA, McCauley JC, Bugbee WD. Osteochondral allograft transplantation for knee lesions after failure of cartilage repair surgery. *Cartilage*. 2015;6(2):98-105.
20. Gross AE, Aubin P, Cheah HK, Davis AM, Ghazavi MT. A fresh osteochondral allograft alternative. *J Arthroplasty*. 2002;17(4 Suppl 1):50-53.
21. 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.
22. Gudas R, Gudaitė A, Pocius A, et al. Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. *Am J Sports Med*. 2012;40(11):2499-2508.
23. Harris JD, Hussey K, Saltzman BM, et al. Cartilage repair with or without meniscal transplantation and osteotomy for lateral compartment chondral defects of the knee: case series with minimum 2-year follow-up. *Orthop J Sports Med*. 2014;2(10):2325967114551528.
24. Harris JD, Hussey K, Wilson H, et al. Biological knee reconstruction for combined malalignment, meniscal deficiency, and articular cartilage disease. *Arthroscopy*. 2015;31(2):275-282.
25. Harris JD, Siston RA, Brophy RH, Lattermann C, Carey JL, Flanigan DC. Failures, re-operations, and complications after autologous chondrocyte implantation: a systematic review. *Osteoarthritis Cartilage*. 2011;19(7):779-791.
26. Horton MT, Pulido PA, McCauley JC, Bugbee WD. Revision osteochondral allograft transplantations: do they work? *Am J Sports Med*. 2013;41(11):2507-2511.
27. Kang RW, Friel NA, Williams JM, Cole BJ, Wimmer MA. Effect of impaction sequence on osteochondral graft damage: the role of repeated and varying loads. *Am J Sports Med*. 2010;38(1):105-113.
28. Kartus J, Magnusson L, Stener S, Brandsson S, Eriksson BI, Karlsson J. Complications following arthroscopic anterior cruciate ligament reconstruction: a 2-5-year follow-up of 604 patients with special emphasis on anterior knee pain. *Knee Surg Sports Traumatol Arthrosc*. 1999;7(1):2-8.
29. McCormick F, Harris JD, Abrams GD, et al. Trends in the surgical treatment of articular cartilage lesions in the United States: an analysis of a large private-payer database over a period of 8 years. *Arthroscopy*. 2014;30(2):222-226.
30. McCormick F, Harris JD, Abrams GD, et al. Survival and reoperation rates after meniscal allograft transplantation: analysis of failures for 172 consecutive transplants at a minimum 2-year follow-up. *Am J Sports Med*. 2014;42(4):892-897.
31. McCulloch PC, Kang R, Cole BJ. Osteochondral allografts for large defects in the knee. *Tech Knee Surg*. 2006;5(3):165-173.
32. McCulloch PC, Kang RW, Sobhy MH, Hayden JK, Cole BJ. Prospective evaluation of prolonged fresh osteochondral allograft transplantation of the femoral condyle: minimum 2-year follow-up. *Am J Sports Med*. 2007;35(3):411-420.

33. 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.
34. Miller DJ, Smith MV, Matava MJ, Wright RW, Brophy RH. Microfracture and osteochondral autograft transplantation are cost-effective treatments for articular cartilage lesions of the distal femur. *Am J Sports Med*. 2015;43(9):2175-2181.
35. Montgomery S, Foster B, Ngo S, et al. Trends in the surgical treatment of articular cartilage defects of the knee in the United States. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(9):2070-2075.
36. Nosewicz TL, Reilingh ML, van Dijk CN, Duda GN, Schell H. Weight-bearing ovine osteochondral defects heal with inadequate subchondral bone plate restoration: implications regarding osteochondral autograft harvesting. *Knee Surg Sports Traumatol Arthrosc*. 2012;20(10):1923-1930.
37. Paul J, Sagstetter A, Kriner M, Imhoff AB, Spang J, Hinterwimmer S. Donor-site morbidity after osteochondral autologous transplantation for lesions of the talus. *J Bone Joint Surg Am*. 2009;91(7):1683-1688.
38. Paxton ES, Stock MV, Brophy RH. Meniscal repair versus partial meniscectomy: a systematic review comparing reoperation rates and clinical outcomes. *Arthroscopy*. 2011;27(9):1275-1288.
39. Pylawka TK, Wimmer M, Cole BJ, Virdi AS, Williams JM. Impaction affects cell viability in osteochondral tissues during transplantation. *J Knee Surg*. 2007;20(2):105-110.
40. Reddy S, Pedowitz DI, Parekh SG, Sennett BJ, Okereke E. The morbidity associated with osteochondral harvest from asymptomatic knees for the treatment of osteochondral lesions of the talus. *Am J Sports Med*. 2007;35(1):80-85.
41. Richter DL, Schenck RC Jr, Wascher DC, Treme G. Knee articular cartilage repair and restoration techniques: a review of the literature. *Sports Health*. 2016;8(2):153-160.
42. Rue JP, Yanke AB, Busam ML, McNickle AG, Cole BJ. Prospective evaluation of concurrent meniscus transplantation and articular cartilage repair: minimum 2-year follow-up. *Am J Sports Med*. 2008;36(9):1770-1778.
43. Saris DBF, Vanlauwe J, Victor J, et al. Treatment of symptomatic cartilage defects of the knee: characterized chondrocyte implantation results in better clinical outcome at 36 months in a randomized trial compared to microfracture. *Am J Sports Med*. 2009;37(1 Suppl):10S-19S.
44. Sherman SL, Garrity J, Bauer K, Cook J, Stannard J, Bugbee W. Fresh osteochondral allograft transplantation for the knee: current concepts. *J Am Acad Orthop Surg*. 2014;22(2):121-133.
45. Steinhoff AK, Bugbee WD. Outcomes of total knee arthroplasty after osteochondral allograft transplantation. *Orthop J Sports Med*. 2014;2(9):2325967114550276.
46. van Dijk CN, Reilingh ML, Zengerink M, van Bergen CJ. Osteochondral defects in the ankle: why painful? *Knee Surg Sports Traumatol Arthrosc*. 2010;18(5):570-580.