Do Outcomes of Osteochondral Allograft Transplantation Differ Based on Age and Sex?

A Comparative Matched Group Analysis

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Background: The effect of patient age or sex on outcomes after osteochondral allograft transplantation (OCA) has not been assessed.

Purpose: To determine clinical outcomes for male and female patients aged ≥40 years undergoing OCA compared with a group of patients aged <40 years.

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

Methods: A review of prospectively collected data of consecutive patients who underwent OCA by a single surgeon with a minimum follow-up of 2 years was conducted. The reoperation rate, failure rate, and patient-reported outcome scores were reviewed. All outcomes were compared between patients aged <40 or ≥40 years, with subgroup analyses conducted based on patient sex. Failure was defined as revision OCA, conversion to knee arthroplasty, or gross appearance of graft failure at second-look arthroscopic surgery. Descriptive statistics, Fisher exact or chi-square testing, and Mann-Whitney *U* testing were performed, with $P <$ .05 set as significant.

Results: A total of 170 patients (of 212 eligible patients; 80.2% follow-up) who underwent OCA with a mean follow-up of 5.0 ± 2.7 years (range, 2.0-15.1 years) were included, with 115 patients aged <40 years (mean age, 27.6 ± 7.3 years; 58 male, 57 female) and 55 patients aged ≥40 years (mean age, 44.9 ± 4.0 years; 33 male, 22 female). There were no differences in the number of pre-OCA procedures between the groups (P = .085). There were no differences in the reoperation rate (<40 years: 38%; ≥40 years: 36%; P = .867), time to reoperation (<40 years: 2.12 ± 1.90; ≥40 years: 3.43 ± 3.43; P = .126 [AQ: 1]), or failure rate (<40 years: 13%; ≥40 years: 16%; P = .639) between the older and younger groups. Patients in both groups demonstrated significant improvement in Lysholm (<40 years: $P <$ .001; ≥40 years: $P <$ .001), International Knee Documentation Committee (IKDC) (<40 years: $P <$ .001; ≥40 years: $P <$ .001), Knee Injury and Osteoarthritis Outcome Score (KOOS) (<40 years: $P <$ .001; ≥40 years: $P <$ .001), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (<40 years: $P <$ .001; ≥40 years: $P <$ .001), and Short Form–12 (SF-12) physical (<40 years: $P <$ .001; ≥40 years: $P <$ .001) scores compared with preoperative values. Patients aged ≥40 years demonstrated significantly higher KOOS symptom (P = .015) subscores compared with patients aged <40 years. There were no significant differences in the number of complications, outcome scores, or time to failure between the sexes. Of the failed patients, female patients aged <40 years failed significantly earlier than male patients (P = .039), while male patients aged ≥40 years failed significantly earlier than female patients (P = .046).

Conclusion: This study provides evidence that OCA is a safe and reliable treatment option for osteochondral defects in patients aged ≥40 years. Male and female patients had similar outcomes. Patients aged <40 years demonstrated lower KOOS symptom subscores postoperatively compared with older patients, potentially attributable to higher expectations of return to function postoperatively as compared with older patients.

Keywords: knee; articular cartilage; meniscus; female athlete; aging athlete

Joint preservation surgery via reparative, reconstructive, and biological techniques has become increasingly utilized over the past 2 decades.[12-14] The main goals of treatment for patients with symptomatic articular cartilage lesions are to improve function and reduce pain. The volume of young athletic patients with symptomatic articular cartilage

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lesions combined with the growth of older patients wishing to remain highly active as they age has increased the need for nonarthroplasty alternatives for the management of articular cartilage abnormalities. While excellent at reducing pain and improving long-term function, knee arthroplasty can result in wear-related complications as well as the need for ≥1 revision procedures over a patient's lifetime, particularly for younger patients. As a result, many patients request nonarthroplasty and joint-preserving solutions for the management of articular cartilage lesions and/or meniscus deficiency.

Selecting the most appropriate cartilage procedure for a given patient involves consideration of a myriad of patient-specific and lesion-specific variables. Several investigators have identified demographic, preoperative, intraoperative, and postoperative factors associated with a good or poor outcome for a multitude of cartilage restoration procedures.[9,20,21] These factors include, but are not limited to, body mass index (BMI), smoking status, workers' compensation status, symptom duration, quantity and type of prior knee procedures, activity level, medical comorbidities, concomitant knee lesion, and size and location of cartilage damage. Joint preservation procedures for articular cartilage defects include microfracture, autologous chondrocyte implantation (ACI), osteochondral autograft transplantation (OATS), and osteochondral allograft transplantation (OCA).[1,4,9,15,27] While there is certainly variability within the literature, the age of patients undergoing articular cartilage restoration via any of these techniques averages approximately 25 to 35 years,[3,10] with very little data available that are applicable to "older" patients. In addition, the demographic characteristics of the patient populations within most cartilage restoration studies include similar numbers of male and female patients, with results often presented as pooled analyses of all included patients and little information on outcomes specific to male versus female patients.

To date, the effect of patient age as an independent risk factor on outcomes and failure rates after OCA of the knee has not been assessed. Similarly, the effect of patient sex on outcomes and failure rates after OCA is also unknown. The purpose of this study was to determine clinical outcomes for male and female patients aged ≥40 years undergoing OCA compared with a group of male and female patients aged <40 years. The authors hypothesized that there would be no differences in patient outcomes based on sex and that the older patients would have inferior clinical outcomes, with higher failure rates, compared with the younger patients.

METHODS

This study was approved by our university's institutional review board. A total of 212 consecutive patients undergoing OCA of the knee joint by a single surgeon between 2003 and 2014 were identified from a prospectively collected database. Inclusion and exclusion criteria are listed in Table 1.

TABLE 1
Inclusion and Exclusion Criteria[a]

Inclusion Criteria	Exclusion Criteria
• OCA of the knee	• Revision OCA
• Senior surgeon	• <15 years of age
• Minimum 2-year follow-up	• Lack of ≥2-year follow-up

[a]OCA, osteochondral allograft transplantation.

Patients were not excluded for having undergone prior ipsilateral knee surgery (other than prior OCA) or for undergoing concomitant procedures at the time of OCA, including meniscus allograft transplantation (MAT), ligament reconstruction, and/or corrective realignment procedures such as high tibial osteotomy or distal femoral osteotomy. Demographic, preoperative, intraoperative, and postoperative data were collected for all patients, as shown in Table 2. For all patients, preoperative and postoperative (minimum 2 years after surgery) validated clinical patient-reported outcome (PRO) scores were collected, including the Lysholm, International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form–12 (SF-12) mental and physical subscales. Outcomes in patients aged ≥40 years were compared with outcomes in patients aged <40 years. Subgroup analyses were also performed to compare between male and female patients within both age groups.

Reoperations and complications were analyzed for patients in both age groups and between sexes. The reoperation rate, timing of reoperation, procedure performed, and findings at the time of reoperation were reviewed. A reoperation was defined as any subsequent surgical procedure on the ipsilateral knee, including surgical debridement, chondroplasty, second-look arthroscopic surgery, hardware removal, revision OCA, or knee arthroplasty. Failure was defined as revision OCA, conversion to knee arthroplasty, or gross appearance of graft failure at second-look arthroscopic surgery.

Surgical Technique

The surgical technique used in this study cohort for OCA has been previously described.[19] All patients underwent this procedure in the supine position under general anesthesia. After an examination under anesthesia, diagnostic arthroscopic surgery was performed to confirm the

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TABLE 2
Data Collected[a]

Demographic	Age, sex, BMI, and insurance status (including workers' compensation status)
Preoperative	Mechanism of original injury, type/level of athlete, and number and type of prior ipsilateral knee surgeries
Intraoperative	Laterality, compartment involved, size of defect relative to size of involved condyle (for femoral condyle procedures), depth of defect, and concomitant procedures performed • OCA with MAT • OCA with realignment procedure (HTO or DFO or AMZ) • OCA with ACL reconstruction • OCA ± MAT ± osteotomy ± ACL reconstruction
Postoperative	Complications, reoperations, and validated patient-reported outcome scores at a minimum of 2 years after surgery

[a]ACL, anterior cruciate ligament; AMZ, anteromedialization; BMI, body mass index; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; MAT, meniscus allograft transplantation; OCA, osteochondral allograft transplantation.

presence of the osteochondral lesion. On the back table, the fresh osteochondral allograft was prepared according to the size of the osteochondral defect. Mini-arthrotomy was performed to prepare the defect site and perform allograft transplantation. For arthrotomy, a midline incision from the superior pole of the patella to the level of the joint line was used for most patients, with the incision extended distally or proximally as needed for patients undergoing concomitant osteotomy. Concomitant ligament reconstruction, MAT, and/or realignment osteotomy procedures were performed as necessary.

Rehabilitation Protocol

The senior author's (B.J.C.) preferred postoperative rehabilitation protocol has also been previously described.[19] In brief, protected weightbearing in a hinged knee brace was required for the first 4 to 6 weeks, followed by progression to full weightbearing as tolerated. Early weightbearing range of motion (0°-90°) was restricted until 4 to 6 weeks after surgery. The brace was discontinued between weeks 4 and 8, pending the patient's quadriceps strength. Patients were permitted to return to sport-specific activities by 4 months after surgery for isolated OCA. In the setting of OCA with combined MAT, ligament reconstruction, and/or osteotomy, the rehabilitation protocol was customized to allow recovery from all procedures while protecting the osteochondral allograft.

Statistical Analysis

Statistical analysis was performed utilizing descriptive statistics, chi-square testing, independent-samples *t* testing, Mann-Whitney *U* testing, and bivariate logistic regression analysis where appropriate. 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, and defect size [AQ: 2]. 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 uncensored (those not yet meeting the endpoint of failure) and censored (those who met failure criteria) patients. A comparison of survival between patients aged <40 years and those aged ≥40 years, as well as between male and female patients, 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

A total of 170 patients who underwent OCA with a mean follow-up of 5.0 ± 2.7 years (range, 2.0-15.1 years) were included (80.2%). There were 115 patients aged <40 years (mean age, 27.6 ± 7.3 years [range, 15.3-39.5 years]; 58 male, 57 female) and 55 patients aged ≥40 years (mean age, 44.9 ± 4.0 years [range, 40.1-54.4 years]; 33 male, 22 female). There were a total of 91 male patients (mean age, 34.2 ± 10.8 years) and 79 female patients (mean age, 32.1 ± 9.6 years). There were no significant differences detected in the number of prior ipsilateral knee surgical procedures between the older and younger groups, with patients aged <40 years having a mean of 2.70 ± 1.91 prior knee surgeries versus 2.13 ± 1.04 for the patients aged ≥40 years (*P* = .085). Similarly, there were no significant differences detected in the number of prior ipsilateral knee surgical procedures between the sexes, with male patients having a mean of 2.46 ± 1.82 prior knee surgeries versus 2.58 ± 1.54 for female patients (*P* = .644). There were 57 female patients aged <40 years (mean age, 27.4 ± 6.8 years), 58 male patients aged <40 years (mean age, 27.8 ± 7.8 years), 22 female patients aged ≥40 years (mean age, 44.1 ± 3.6 years), and 33 male patients aged ≥40 years (mean age, 45.4 ± 4.1 years). The mean number of previous surgical procedures was 2.7 ± 1.6 for female patients aged <40 years, 2.7 ± 2.2 for male patients aged <40 years, 2.3 ± 1.4 for female patients aged ≥40 years, and 2.7 ± 2.2 for male patients aged ≥40 years (*P* = .205). Lesion location within the knee can be

TABLE 3
Lesion Location Based on Age and Sex[a]

	<40 y		≥40 y		
	Female	Male	Female	Male	Total
LFC	34	23	4	6	67
MFC	20	35	17	27	99
Patella	2	0	0	0	2
Trochlea	1	0	1	0	2
Total	57	58	22	33	170

[a]Data are shown as No. LFC, lateral femoral condyle; MFC, medial femoral condyle.

TABLE 4
Patient-Reported Outcome Scores for Overall Cohort Preoperatively and at Final Follow-up[a]

	Preoperative	Final Follow-up	*P* Value
Lysholm	42.62 ± 17.37	63.55 ± 22.85	**<.0001**
IKDC	34.91 ± 14.35	59.24 ± 21.59	**<.0001**
KOOS pain	53.60 ± 17.04	74.60 ± 19.28	**<.0001**
KOOS symptom	54.71 ± 16.34	72.26 ± 18.54	**<.0001**
KOOS ADL	64.77 ± 21.55	83.71 ± 19.00	**<.0001**
KOOS sport	25.50 ± 20.73	50.42 ± 26.55	**<.0001**
KOOS QOL	25.06 ± 18.67	51.88 ± 24.89	**<.0001**
WOMAC pain	7.49 ± 3.90	3.96 ± 3.71	**<.0001**
WOMAC stiffness	3.61 ± 1.81	2.33 ± 1.82	**<.0001**
WOMAC function	23.96 ± 14.6	10.58 ± 12.12	**<.0001**
WOMAC overall	2.96 ± 1.70	6.24 ± 2.72	**<.0001**
Symptom rate	4.35 ± 1.95	6.81 ± 2.23	**<.0001**
SF-12 physical	43.41 ± 7.45	43.41 ± 7.40	**<.0001**
SF-12 mental	51.36 ± 11.40	52.70 ± 11.74	.394

[a]Data are shown as mean ± SD. ADL, activities of daily living; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; QOL, quality of life; SF-12, Short Form–12; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index. [AQ: 4]

found in Table 3. Female patients aged <40 years had a mean lesion size of 406.0 ± 181.1 cm^2, male patients aged <40 years had a mean lesion size of 493.2 ± 179.4 cm^2, female patients aged ≥40 years had a mean lesion size of 411.1 ± 160.3 cm^2, and male patients aged ≥40 years had a mean lesion size of 489.1 ± 190.2 cm^2. When comparing defect-to-condyle size ratios between the 4 groups (male <40 years, female <40 years, male ≥40 years, and female ≥40 years), there were no significant differences (P = .667).

There were several demographic and intraoperative differences between the sexes and between the older and younger patient groups. Specifically, the patients aged ≥40 years demonstrated a significantly higher BMI (<40 years: 25.94 ± 5.02 kg/m^2; ≥40 years: 28.11 ± 5.22 kg/m^2; P = .018), had a significantly higher prevalence of workers' compensation claims (<40 years: 19/113 [17%]; ≥40 years: 18/35 [33%]; P = .028 [AQ: 3]), and had a significantly lower prevalence of concomitant distal femoral osteotomy (<40 years: 9/115 [8%]; ≥40 years: 0/55 [0%]; P = .028). In addition, male patients had a significantly higher BMI overall (27.72 ± 4.32 kg/m^2 vs 25.36 ± 5.81 kg/m^2, respectively; P = .004) as well as on subanalysis by age ≥40 years (29.38 ± 3.68 kg/m^2 vs 26.09 ± 6.64 kg/m^2, respectively; P = .026) compared with female patients. The overall cohort demonstrated significant improvements in Lysholm, IKDC, KOOS, WOMAC, and SF-12 physical scores as compared with preoperative values (P < .05 for all) (Table 4).

Analysis Based on Age

At final follow-up, there were no overall differences detected in the reoperation rate (<40 years: 38%; ≥40 years: 36%; P = .867), time to reoperation (<40 years: 2.12 ± 1.90; ≥40 years: 3.43 ± 3.43; P = .126 [AQ: 5]), or failure rate (<40 years: 13%; ≥40 years: 16%; P = .639) between the older and younger patients. Patients in both groups demonstrated significant improvement in Lysholm (<40 years: P < .001; ≥40 years: P < .001), IKDC (<40 years: P < .001; ≥40 years: P < .001), KOOS (<40 years: P < .001; ≥40 years: P < .001), WOMAC (<40 years: P < .001; ≥40 years: P < .001), and SF-12 physical (<40 years: P < .001; ≥40 years: P < .001) scores compared with preoperative values. Postoperative SF-12 mental subscores were not significantly improved at final follow-up for either group (P > .05 for both groups). Comparatively, the older group demonstrated significantly higher KOOS symptom (P = .015) subscores compared with the younger group at final follow-up (Figure 1).

There was a significant difference in the number of patients aged <40 years undergoing concomitant lateral MAT (27 vs 1, respectively; P < .0001) and distal femoral osteotomy (9 vs 0, respectively; P = .033) compared with patients aged ≥40 years. There were no other significant differences in concomitant procedures between the groups. Similarly, there were no significant differences in the number of prior failed cartilage procedures, number of complications, or time to failure between the younger and older groups (Figure 2 and Table 5).

Subgroup Analysis Based on Sex

Both male and female patients demonstrated significant improvements in postoperative Lysholm, IKDC, KOOS, WOMAC, and SF-12 physical scores as compared with preoperative values (P < .05 for both groups). There were no significant differences in any PRO scores between the sexes at final follow-up (Figure 3).

Overall, compared with male patients, female patients were significantly more likely to have failed prior ACI (P = .031), significantly more likely to undergo concomitant lateral MAT (P = .004), and significantly less likely to undergo concomitant high tibial osteotomy (P = .031). There were no significant differences in the number of complications or time to failure between the sexes (Figure 4).

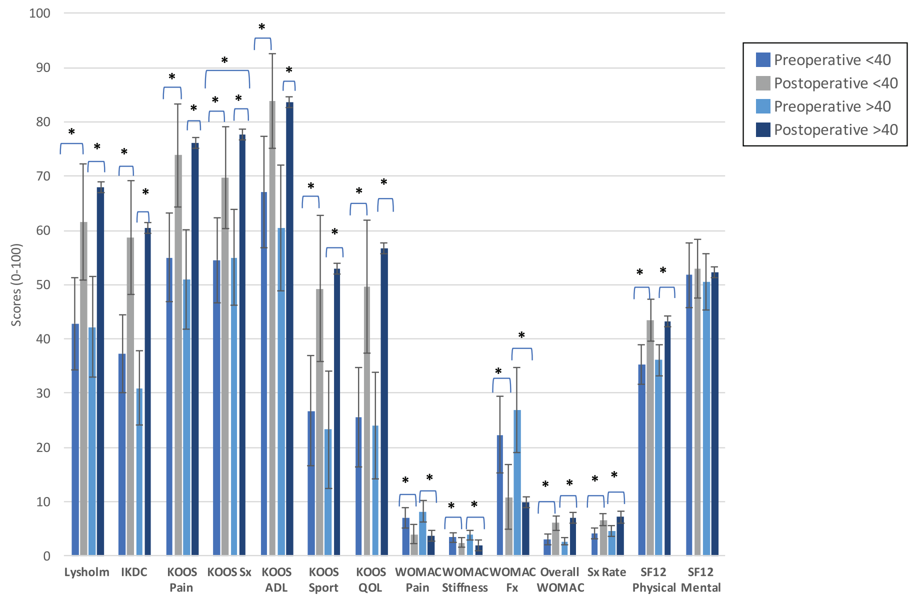

Figure 1. Summary of patient-reported outcome scores at a mean follow-up of 5.0 ± 2.7 years. Patients in both age groups demonstrated significant improvements in Lysholm, International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form–12 (SF-12) physical scores as compared with preoperative values ($P < .05$ for both groups as indicated by the small brackets and asterisks). Postoperative SF-12 mental subscores were not significantly improved at final follow-up for either group ($P >$ .05 for both groups). Patients aged ≥40 years demonstrated significantly higher KOOS symptom (P = .015) subscores compared with patients aged <40 years as indicated by the wider bracket with asterisk.

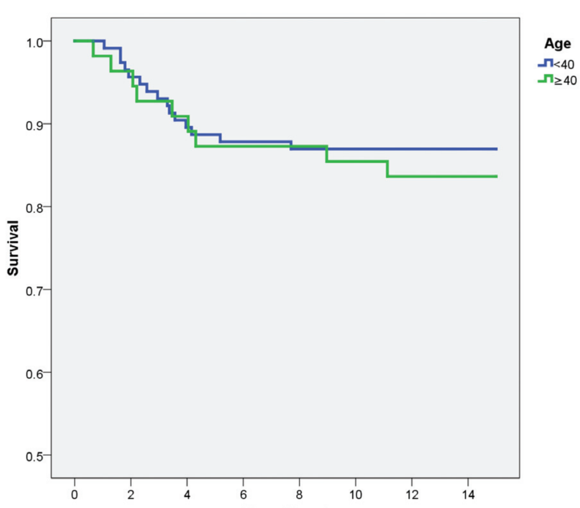

Figure 2. Kaplan-Meier survival probabilities were obtained for failed grafts, with patients aged ≥40 years demonstrating a mean time to failure of 4.239 years while patients aged <40 years had a mean time to failure of 3.140 years. Survival probabilities at 1, 2, 3, 5, and 10 years, respectively, were 98.2%, 96.4%, 92.7%, 87.3%, and 85.5% for patients aged ≥40 years and 100.0%, 95.7%, 93.0%, 88.7%, and 87.0% for patients aged <40 years. The log-rank test demonstrated no significant difference in survival distributions between the groups (P = .268).

Subgroup Analysis Based on Age and Sex

Upon additional analysis incorporating both age and sex, female patients aged <40 years were significantly more likely to undergo concomitant lateral MAT (P = .013), while male patients aged <40 years were significantly more likely to undergo concomitant medial MAT (P = .027). No similar differences were found when comparing between male and female patients aged ≥40 years (Table 6). There were no significant differences in final PRO scores between male and female patients aged ≥40 years, while a significant difference (P = .028) was noted for SF-12 physical subscores between male and female patients aged <40 years (Figure 5 and Table 7).

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 OCA (including concomitant MAT), and defect size was independently predictive of reoperations (OR, 1.523 [95% CI, 1.173-1.978]; P = .002) [AQ: 7].

If a patient underwent a reoperation, the number of previous surgical procedures (OR, 2.242 [95% CI, 1.239-4.057]; P = .008) and BMI (OR, 1.194 [95% CI, 1.021-1.396]; P = .027) were predictive of failure. When the cohort was taken as a whole regardless of reoperations, the number of previous surgical procedures (OR, 1.698 [95% CI, 1.207-2.389];

TABLE 5
Involved Compartment and Major Concomitant Procedures Based on Age[a]

	<40 y	≥40 y	Total	*P* Value
Involved compartment				**.001**
Medial femoral condyle	55 (32.4)	44 (25.9)	99 (58.2)	
Lateral femoral condyle	57 (33.5)	10 (5.9)	67 (39.4)	
Patella	2 (1.2)	0 (0.0)	2 (1.2)	
Trochlea	1 (0.6)	1 (0.6)	2 (1.2)	
Any concomitant procedure				.418
No	53 (46.1)	29 (52.7)	82 (48.2)	
Yes	62 (53.9)	26 (47.3)	88 (51.8)	
Ligament repair or reconstruction				.971
No	113 (98.3)	54 (98.2)	167 (98.2)	
Yes	2 (1.7)	1 (1.8)	3 (1.8)	
MAT				.297
No	70 (60.9)	38 (69.1)	108 (63.5)	
Yes	45 (39.1)	17 (30.9)	62 (36.5)	
Lateral MAT				**<.0001**
No	88 (76.5)	54 (98.2)	142 (83.5)	
Yes	27 (23.5)	1 (1.8)	28 (16.5)	
Medial MAT				.058
No	96 (83.5)	39 (70.9)	135 (79.4)	
Yes	19 (16.5)	16 (29.1)	35 (20.6)	
HTO				.215
No	107 (93.0)	48 (87.3)	155 (91.2)	
Yes	8 (7.0)	7 (12.7)	15 (8.8)	
DFO				**.033**
No	106 (92.2)	55 (100.0)	161 (94.7)	
Yes	9 (7.8)	0 (0.0)	9 (5.3)	
AMZ				.227
No	112 (97.4)	55 (100.0)	167 (98.2)	
Yes	3 (2.6)	0 (0.0)	3 (1.8)	

[a]Data are shown as n (%). AMZ, anteromedialization; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; MAT, meniscus allograft transplantation.

P = .002) and BMI (OR, 1.146 [95% CI, 1.024-1.282]; *P* = .018) were predictive of failure in general. While as noted above, the number of prior ipsilateral knee surgical procedures was not significantly different between the 4 groups, male patients as well as patients aged ≥40 years did have a higher BMI relative to the other groups.

The overall failure rate for patients aged <40 years was 13% (n = 15), while the overall failure rate for patients aged ≥40 years was 16% (n = 9). In patients aged <40 years, female patients who failed experienced failure significantly more quickly than male patients (1.90 ± 0.60 years after OCA vs 3.76 ± 1.73 years after OCA, respectively; *P* = .039). In contrast, in patients aged ≥40 years, male patients who failed experienced failure significantly more quickly than female patients (2.64 ± 1.51 years after OCA vs 7.44 ± 4.63 years after OCA, respectively; *P* = .046) (Figure 6).

DISCUSSION

The principal findings of this study demonstrate that (1) patients aged ≥40 years undergoing OCA had similar survival and reoperation rates at 5 years after surgery compared with younger patients; (2) female patients aged <40 years tended to fail significantly earlier than male patients, while male patients aged ≥40 years tended to fail significantly earlier than female patients; and (3) patients aged ≥40 years had significantly higher postoperative KOOS symptom subscores (higher scores correspond to less symptoms) after OCA compared with younger patients, potentially attributable to higher expectations of return to function after surgery. The findings from this study did not support our hypotheses, as older patients did not have inferior outcomes, nor did they have higher failure rates compared with younger patients, and further, there were no differences in PRO scores based on patient sex. Overall, these data can be used to counsel patients when being offered OCA as part of a knee joint preservation strategy.

Indications for knee joint preservation surgery are continuously evolving. In many cases, procedures such as OCA are considered “salvage” surgeries, as they are performed as a final effort to reduce pain and improve function for simple activities of daily living in patients with debilitating knee pain and dysfunction. In other cases, these procedures are performed in an effort to return patients to recreational/sport activities that they otherwise are unable to participate in because of large symptomatic osteochondral lesions. Certainly, one of the main concerns

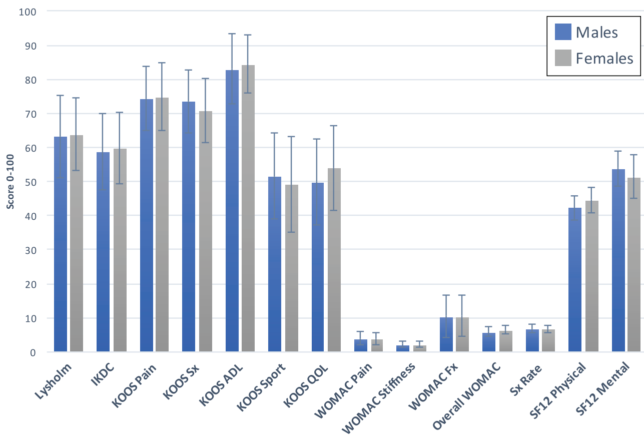

Figure 3. Summary of male versus female patient-reported outcome (PRO) scores at a mean follow-up of 5.0 ± 2.7 years. Patients of both sexes demonstrated significant improvements in Lysholm, International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form–12 (SF-12) physical scores as compared with preoperative values ($P <$ .05 for both groups). Postoperative SF-12 mental subscores were not significantly improved at final follow-up for either group ($P >$ .05 for both groups). There were no significant differences in any PRO scores at final follow-up.

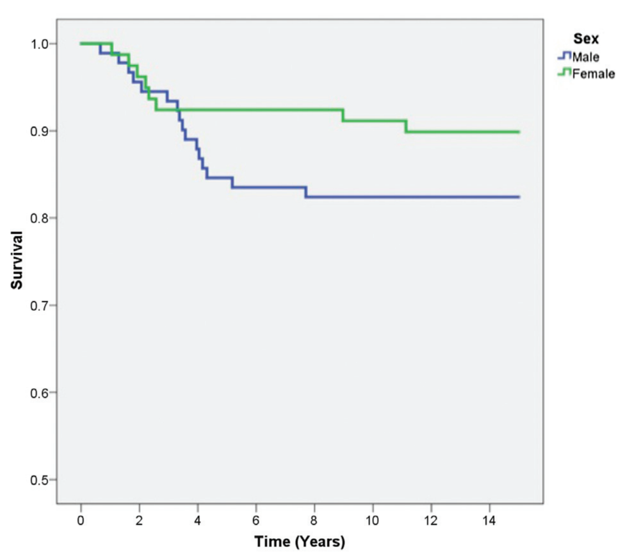

Figure 4. Kaplan-Meier survival probabilities were obtained for failed grafts stratifying by sex, with male patients demonstrating a mean time to failure of 3.341 years while female patients had a mean time to failure of 3.975 years. Survival probabilities at 1, 2, 3, 5, and 10 years, respectively, were 98.9%, 95.6%, 93.4%, 84.6%, and 82.4% for male patients and 100.0%, 96.2%, 92.4%, 92.4%, and 91.1% for female patients. The log-rank test demonstrated no significant difference in survival distributions between the groups (P = .716).

TABLE 6
Concomitant Procedures Based on Age and Sex[a]

	<40 y			≥40 y		
	Male	Female	*P* Value	Male	Female	*P* Value
Any concomitant Procedure			.92			.741
No	27	26		18	11	
Yes	31	31		15	11	
Ligament repair or reconstruction			.15			.41
No	58	55		32	22	
Yes	0	2		1	0	
MAT			.79			.19
No	36	34		25	13	
Yes	22	23		8	9	
Lateral MAT			**.013**			.216
No	50	38		33	21	
Yes	8	19		0	1	
Medial MAT			**.027**			.332
No	44	52		25	14	
Yes	14	5		8	8	
HTO			.15			.137
No	52	55		27	21	
Yes	6	2		6	1	
DFO			.708			>.99
No	54	52		33	22	
Yes	4	5		0	0	
AMZ			.077			>.99
No	58	54		33	22	
Yes	0	3		0	0	

[a]Data are shown as No. AMZ, anteromedialization; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; MAT, meniscus allograft transplantation. [AQ: 6]

for patients undergoing OCA is the durability of the procedure and its potential to delay and/or avoid the need for future knee surgery, particularly knee arthroplasty. This concern may be especially relevant for patients who are older than the typical patient undergoing joint preservation surgery but younger than the typical patient undergoing knee arthroplasty. These patients are often unfortunately living in between the "ideal" indications for both types of surgery and are thus trapped in a difficult situation, forced to live with pain/dysfunction until they are "old enough" for knee arthroplasty. Before the present study, the ability of OCA to improve function, reduce pain, and improve the overall quality of life in these "older" patients has been unclear.

Several investigators have reported on clinical outcomes after other joint preservation and cartilage/meniscus restoration procedures among different age cohorts to better understand the upper age limits for which these procedures remain viable treatment options. In a study of 61 athletes (29 professional, 32 recreational) treated with microfracture for isolated knee chondral defects with an average 15-year follow-up, Gobbi et al[8] reported an absolute difference of 1 in overall Tegner scores beginning at 2 years, which was maintained through final follow-up, when comparing patients aged <30 years versus >30

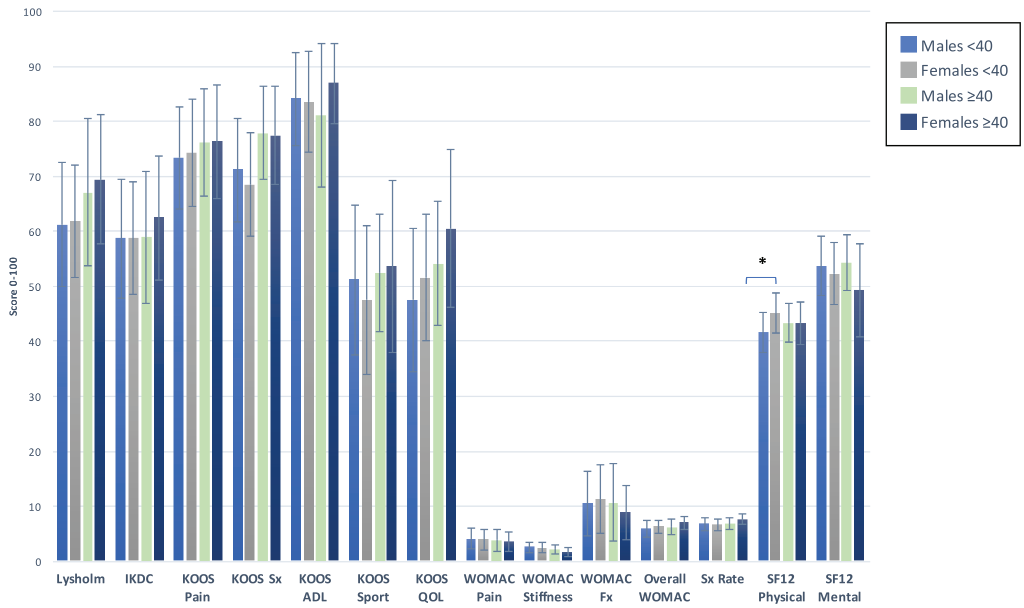

Figure 5. Summary of patient-reported outcome scores at a mean follow-up of 4.80 ± 2.7 years for male patients aged <40 years, 4.63 ± 2.1 years for female patients aged <40 years, 5.94 ± 3.2 years for male patients aged ≥40 years, and 4.84 ± 2.9 years for female patients aged ≥40 years. Patients of both sexes demonstrated significant improvements in Lysholm, International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form–12 (SF-12) physical scores as compared with preoperative values (except female patients aged ≥40 years for WOMAC pain and SF-12 physical) ($P < .05$ for both groups). Postoperative SF-12 mental subscores were not significantly improved at final follow-up for either group ($P > .05$ for both groups).

TABLE 7
Patient-Reported Outcome Scores Based on Age and Sex at Final Follow-up[a]

	<40 y		≥40 y		
	Male	Female	Male	Female	*P* Value
Lysholm	61.20 ± 22.71	61.75 ± 20.48	67.04 ± 26.73	69.42 ± 23.62	.442
IKDC	58.67 ± 21.75	58.75 ± 20.42	58.96 ± 23.88	62.43 ± 22.48	.925
KOOS pain	73.35 ± 18.77	74.31 ± 19.50	76.13 ± 19.65	76.31 ± 20.69	.914
KOOS symptom	71.13 ± 18.81	68.48 ± 18.71	77.91 ± 16.78	77.44 ± 18.02	.095
KOOS ADL	84.06 ± 16.96	83.54 ± 18.15	81.16 ± 26.11	86.92 ± 14.52	.792
KOOS sport	51.17 ± 27.25	47.50 ± 26.89	52.50 ± 21.32	53.68 ± 31.31	.778
KOOS QOL	47.53 ± 26.22	51.56 ± 23.05	54.17 ± 22.53	60.53 ± 28.65	.263
WOMAC pain	4.13 ± 3.65	4.01 ± 3.75	3.85 ± 4.04	3.53 ± 3.55	.944
WOMAC stiffness	2.52 ± 1.94	2.47 ± 1.82	2.18 ± 1.57	1.68 ± 1.80	.338
WOMAC function	10.50 ± 11.61	11.21 ± 12.49	10.69 ± 14.19	8.89 ± 9.87	.918
WOMAC overall	5.88 ± 2.98	6.31 ± 2.49	6.22 ± 2.89	7.00 ± 2.45	.503
Symptom rate	6.77 ± 2.44	6.53 ± 2.12	6.85 ± 2.31	7.65 ± 1.75	.395
SF-12 physical	41.64 ± 7.35	45.13 ± 7.47	43.35 ± 7.13	43.28 ± 7.59	.140
SF-12 mental	53.70 ± 10.66	52.23 ± 11.33	54.23 ± 10.14	49.29 ± 16.78	.479

[a]Data are shown as mean ± SD. ADL, activities of daily living; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; QOL, quality of life; SF-12, Short Form–12; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

years. In addition, the authors found negative correlations between patients' age and lesion size, Tegner scores, and IKDC subjective scores at final follow-up. They concluded that athletes aged >31 years [AQ: 8] with defects greater than 400 mm^2 tend to have inferior outcomes compared with younger athletes treated with microfracture, as demonstrated by significantly lower KOOS, visual analog scale, and Marx scores.[8] In 2 separate publications, Gudas

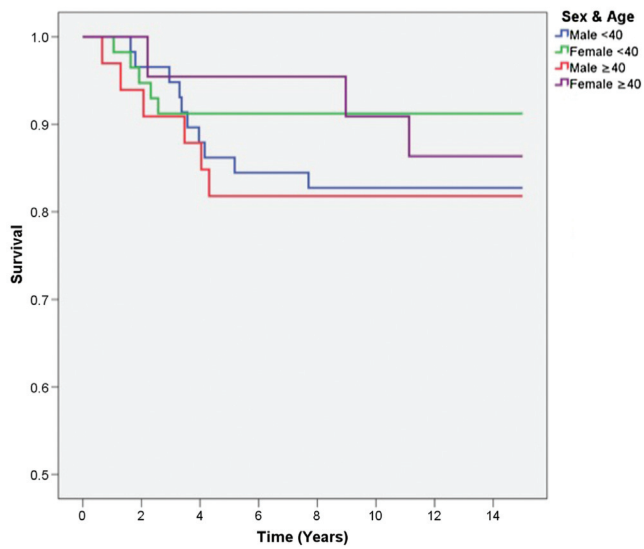

Figure 6. Kaplan-Meier survival probabilities stratifying male and female patients aged <40 and ≥40 years were obtained for failed grafts. The different groups demonstrated mean times to failure of 3.761 years for male patients aged <40 years, 1.898 years for female patients aged <40 years, 2.640 years for male patients aged ≥40 years, and 7.437 years for female patients aged ≥40 years. Survival probabilities at 1, 2, 3, 5, and 10 years, respectively, were 100.0%, 96.6%, 94.8%, 86.2%, and 82.8% for male patients aged <40 years; 100.0%, 96.5%, 91.2%, 91.2%, and 91.2% for female patients aged <40 years; 97.0%, 93.9%, 90.9%, 81.8%, and 81.8% for male patients aged ≥40 years, and 100.0%, 94.7%, 91.2%, 91.2%, and 91.2% for female patients aged ≥40 years. The log-rank test demonstrated a significant difference in survival distributions between the groups (*P* = .010).

et al[11,12] described similar findings, namely, that microfracture as well as OATS resulted in significantly better PRO scores in athletes aged <25 years compared with athletes aged >25 years. In a systematic review of 28 studies (level of evidence I-IV) incorporating over 3000 patients (average age, 39 years) undergoing microfracture with an average 41-month follow-up, Mithoefer et al[21] reported that patients aged <40 years had significantly better clinical outcome scores and better cartilage defect fill on magnetic resonance imaging (MRI) than patients aged >40 years. Overall, older age appears to be a risk factor for poor outcomes after microfracture, although the effect of patient age on microfracture failure rates is still unclear.

Similar studies have been conducted to evaluate age-related differences in clinical outcomes in patients undergoing ACI for chondral lesions of the knee. Krishnan et al[17] and Nawaz et al[22] have both reported superior clinical outcomes after ACI in younger patients. In the study by Krishnan and colleagues,[17] 199 patients were prospectively analyzed at 4 years after ACI utilizing the modified Cincinnati score. The authors analyzed the patients within 3 different age groups: patients aged ≤20 years, patients aged 21 to 40 years, and patients aged ≥41 years. The authors found good to excellent clinical results in 86% of patients in the ≤20-year group, 64% in the 21-to-40–year group, and 56% in the ≥41-year group. Nawaz et al[22] reported on 827 patients who underwent ACI or matrix-assisted ACI at an average of 6.2-year follow-up. The authors reported that younger patients were significantly more likely to have longer graft survival durations versus older patients, with a hazard ratio of 1.039 for age at the time of surgery favoring younger patients.[22] In contrast, Niemeyer and colleagues[23] found that several PRO scores (IKDC, Lysholm, Cincinnati, and Tegner) in patients aged >40 years were similar to those of younger patients at an average 2-year follow-up. In a separate study, Rosenberger et al[26] evaluated clinical outcomes of ACI in 56 patients aged >45 years with a minimum 2-year follow-up. Interestingly, the authors found a similar failure rate (14%) of ACI in their cohort when compared to previous studies of younger cohorts, including a 13% failure rate found in a study by Browne et al.[2] Other authors have evaluated the effect of age on return to activity and return to sport after ACI, noting a quicker return to activity/return to sport and superior clinical outcomes in patients aged <30 years compared with older patients.[5,24] Pestka and colleagues[24] reported on 130 patients with isolated full-thickness cartilage defects of the knee treated with ACI and found that patients aged <30 years returned to work, on average, 4.1 weeks earlier than patients aged between 30 and 45 years. Interestingly, the authors reported a significant difference in patient-reported improvement in the ability to perform sporting activities, with 70% of patients aged >50 years reporting improvement versus only 29% of patients aged <30 years (*P* = .042). Similar to the findings in the present study, younger patients may have higher postoperative expectations for returning to sport/activity when compared with older patients, who may simply be more satisfied with lower levels of activities, especially if those activities can be performed with minimal to no pain. However, other authors have presented conflicting data. For example, Filardo et al[5] reported superior clinical outcome scores and return-to-activity rates in patients aged <20 years compared with patients aged >40 years in a series of 133 patients treated with matrix-assisted ACI (*P* =< .0005 [AQ: 9]).

Knutsen and colleagues[13-15] conducted a randomized controlled trial comparing the outcomes of patients undergoing ACI (n = 40) to those undergoing microfracture (n = 40). Patients in this study ranged from 18 to 45 years of age. In their initial report,[4] the authors found that patients aged <30 years, regardless of the treatment group, had significantly superior PRO scores compared with older patients at 2 years after surgery. In addition, at 5 years after surgery,[14] these results were maintained, with patients aged <30 years having superior clinical outcomes compared with the older patients. In their most recent publication describing the outcomes of these patients at long-term follow-up (average, 14 years),[13] the authors did not describe differences in outcomes as related to age, with general failure rates ranging between 30% and 45%. Their early results demonstrate a greater likelihood of a good clinical outcome in younger patients undergoing microfracture or ACI; however, the long-term efficacy of both ACI and microfracture for the treatment of focal cartilage defects in the knee appears limited.

Similar to microfracture and ACI, several investigators have evaluated age-related clinical outcomes of OATS. In their analysis of 55 patients undergoing OATS at an average 5.9-year follow-up, Robb et al[25] demonstrated improved Oxford knee scores in younger patients based on linear regression analysis. Interestingly, as part of a systematic review of 55 studies comprising 2459 patients treated with either ACI, microfracture, OATS, or OCA, Krych et al[18] conducted a meta-regression analysis in an attempt to identify variables associated with good or poor outcomes. The authors demonstrated that neither age nor lesion size had a significant effect on athletes' ability to return to sport.[18] Overall, while some authors have demonstrated that younger patients/athletes have better outcomes after cartilage restoration procedures, other studies have shown no such differences. In the present study, age was not an independent risk factor for reoperations, complications, failures, or overall outcomes. We hypothesize that this is in part because of the consistent utilization of strict indications for surgery by the senior author, which prohibited patients with diffuse arthritic changes (who are likely to be older) from undergoing OCA. Certainly, additional work on the effect of age as an independent risk factor for poor outcomes and/or failure after ACI, microfracture, and OATS is needed.

Studies analyzing the effect of patient sex on outcomes after cartilage restoration are extremely limited. In 2013, Kreuz et al[16] described clinical and MRI outcomes in 25 male and 27 female patients with an average age of 36 years undergoing ACI for full-thickness chondral defects of the knee. Interestingly, the authors found that at 6, 12, and 48 months after surgery, male patients had significantly better Lysholm scores compared with female patients and further found that female patients with patellar defects had the worst overall outcomes. Notably, no significant differences in defect fill as seen on MRI were found between the male and female patients. This is in contrast to our study in which there were no significant differences in PRO scores at final follow-up when comparing male and female patients.

In the present cohort of 170 patients, there were no differences in PRO scores, reoperation rates, or failure rates between male and female patients, suggesting that patient sex does not affect overall outcomes after OCA. Interestingly, among patients aged <40 years who failed OCA (overall failure rate, 13%), female patients failed at a mean 1.90 years after index OCA, nearly 2 years earlier than male patients, who experienced failure at a mean 3.76 years after OCA. In contrast, among patients aged ≥40 years who failed OCA (overall failure rate, 16%), male patients failed at a mean 2.64 years after index OCA, just under 5 years earlier than female patients, who experienced failure at 7.44 years after index OCA. It is unclear as to why younger female patients failed earlier than younger male patients or why older male patients failed earlier than older female patients, especially as overall PRO scores were similar between the groups.

Determining the effect of age on outcomes and revision rates after OCA of the knee is helpful in determining if OCA should even be offered to patients beyond a certain age limit. Unfortunately, this is an extremely complex clinical question, and there is no literature available that compares the outcomes, complications, revisions, or cost-effectiveness of OCA versus other joint preservation procedures or versus knee arthroplasty in an older patient population.

Certainly, OCA is not a benign procedure, and several authors[6,28] have demonstrated inferior clinical outcomes with higher failure rates after knee arthroplasty in the setting of prior OCA compared with historical reports of outcomes after knee arthroplasty in patients without prior cartilage restoration. The present study found that overall graft survival rates, complication rates, and reoperation rates in patients aged ≥40 years undergoing OCA were similar compared with outcomes in younger patients, suggesting that at medium-term follow-up (mean, 5 years), older age is not a negative prognostic factor. Further, these data suggest that patient sex is not a prognostic factor for success or failure, as both male and female patients performed equally well after OCA. Given that the majority of available studies on OCA and articular cartilage restoration in general describe patients with an average age of approximately 25 to 35 years,[3,10] the findings from the current study will be useful in specifically counseling both male and female patients aged ≥40 years who are being considered for OCA.

Limitations

This study is not without limitations. Patients in the older and younger age groups were not matched in a 1-to-1 format, and thus, variables such as patient sex, BMI, workers' compensation status, number of prior surgical procedures, and/or the presence of concomitant procedures performed at the time of OCA may affect outcomes. Fortunately, there were no differences in the number of prior knee surgical procedures in the <40-year and ≥40-year groups, a variable that has been shown to be a negative prognostic factor for reoperations and failures after OCA of the knee.[7] Patients aged ≥40 years had a significantly higher BMI and a significantly higher prevalence of workers' compensation claims compared with patients aged <40 years, and thus, both of these variables may represent confounding factors. Given that there were no significant differences in overall graft survival rates, complication rates, and reoperation rates in patients aged <40 years compared with patients aged ≥40 years, the statistical differences in BMI and workers' compensation status between the groups are likely not clinically relevant. There was a relatively large number of patients with workers' compensation claims, which certainly may influence outcomes, although as noted in the logistic regression analysis, workers' compensation status was not an independent risk factor for reoperations, failures, or overall outcomes. Finally, 52% of the cohort underwent concomitant procedure(s) with OCA, and thus, the outcomes and reoperation rates described in this study may have been influenced by the concomitant procedures as opposed to being a reflection of the OCA procedure. As noted in an initial survival analysis of patients undergoing OCA, patients undergoing OCA often have multiple coexisting lesions, including irreparable meniscus abnormalities, malalignment, and/or ligamentous insufficiency, and require multiple procedures in addition to OCA.[7]

CONCLUSION

Patients who require OCA for osteochondral lesions of the knee are extremely difficult to treat. These patients typically present after having undergone at least 1 prior surgical procedure, have high preinjury activity levels, and have high postoperative expectations. Knee arthroplasty is usually considered the last resort, given the higher rates of complications and lower survivability of arthroplasty in young patients. This study provides evidence that OCA is a safe and reliable treatment option for osteochondral defects in patients aged $\geq$40 years. Male and female patients had similar outcomes, although the time to failure differed by both sex and age. Patients aged $<$40 years demonstrated lower KOOS symptom subscores postoperatively compared with older patients, potentially attributable to higher expectations of return to function postoperatively as compared with older patients. Together, these data suggest that at medium-term follow-up, older age is not a negative prognostic factor for both male and female patients undergoing OCA of the knee.

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