Outcomes After Fresh Osteochondral Allograft Transplantation for Medium to Large Chondral Defects of the Knee

Dimitri Thomas,* MD, MAJ (MC USA), K. Aaron Shaw,† DO, CPT(P) (MC USA), and Brian R. Waterman,‡§ MD

Investigation performed at the Dwight D. Eisenhower Army Medical Center, Fort Gordon, Georgia, USA

Background: Articular cartilage defects of the knee can significantly impair function among young, high-demand patients. There are several techniques for chondral restoration, including osteochondral allograft transplantation (OCA), that may alleviate pain and re-create the native anatomy. However, clinical outcomes among athletic cohorts are limited.

Purpose: To evaluate the efficacy and functional outcomes of OCA for medium to large osteochondral defects of the knee in physically active United States military servicemembers.

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

Methods: A military health care database was queried to identify all OCA procedures performed between January 2009 and March 2013. Inclusion criteria were army personnel with a minimum of 2 years' follow-up. Exclusion criteria included incomplete follow-up, inaccurate coding, and nonmilitary status. Variables of interest included sex, age, lesion location, grade and size of the lesion, body mass index, tobacco use, preoperative and postoperative visual analog scale (VAS) scores for pain, and presence of perioperative complications. Overall failure was defined as the inability to return to preoperative functional activities because of persistent knee complaints (clinical failure) or a revision cartilage procedure or arthroplasty (surgical failure).

Results: A total of 61 patients (52 male; mean age, 31.7 years) were identified, with a mean 46.2-month follow-up. The mean VAS pain score improved from 4.10 ± 2.17 preoperatively to 2.68 ± 2.73 postoperatively ($P < .0009$), and only 6 (9.8%) required a subsequent revision chondral procedure. Overall, 39 patients (63.9%) were able to return to a level of activity that allowed for the completion of military duties. Risk factors for clinical failure were preoperative body mass index, preoperative pain as measured on the VAS, and moderate to severe postoperative pain on the VAS. The risk factor for surgical failure was the presence of a complication. Risk factors for overall failure were the presence of a complication and moderate to severe postoperative pain on the VAS.

Conclusion: OCA provided moderate success in retaining active-duty army servicemembers. Approximately two-thirds of patients undergoing OCA were able to return to their preinjury occupational activity, while approximately 57% of patients returned to prior levels without a subsequent revision chondral procedure or arthroplasty.

Keywords: knee articular cartilage; allograft transplantation; military

Articular cartilage defects of the knee are relatively common, occurring in up to 60% of patients undergoing knee arthroscopic surgery.[39] Unfortunately, the treatment of chondral lesions is limited by the poor inherent regenerative capacity of hyaline cartilage,[14] and neglected articular cartilage defects may result in significant pain and eventual arthritic progression. In 2001, Lindahl et al[19] showed through the Swedish health care system that the cost of work time lost because of knee chondral defects over a 10-year period before surgery amounted to approximately US$122,000, whereas the direct cost from medical treatments amounted to almost US$6000. Furthermore, chondral lesions may be even more problematic for younger, more athletic patients who desire to maintain a physically active lifestyle without debilitating symptoms.

Numerous treatment options exist for articular cartilage defects, including debridement, marrow stimulation, osteochondral autograft transfer (OAT), particulated juvenile allograft transplantation, autologous chondrocyte implantation (ACI), and osteochondral allograft transplantation (OCA). With fresh OCA, high levels of viable donor chondrocytes and the surrounding extracellular matrix may be maintained up to 28 days after the harvest using current guidelines.[40] Newer methods have allowed for an increased

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time between graft harvest and implantation, thereby potentially expanding the pool of allografts available for use.[7,38] Advantages of this technique include the lack of donor site morbidity, the transfer of mature articular cartilage, and the ability to treat larger lesions via autograft transfer. Newly published findings in a canine model have shown that 12 months after surgery, there are no significant differences between allograft and autograft sources in terms of biomechanical properties, osseous integration, gross morphology, and overall histology.[22] In addition, the involvement of subchondral bone in chondral defects is common and has been shown to decrease the efficacy of surface-based treatments such as ACI.[30] Fresh allograft transfer has the ability to address the entire subchondral unit as well as the ability to address sizable lesions unsuitable for autograft transfer, making it an appealing alternative for defects in young, active populations.

Numerous studies have shown good to excellent results of OCA among broader demographics.[2,6,12] However, comparable investigations detailing the outcomes among athletes or other high-demand patient subsets are limited, with less predictable clinical results.[35,36] The purpose of this study was to evaluate the functional outcomes and short-term (2- to 6-year follow-up) revision rate of OCA performed within a physically active military population. Military servicemembers are often required to perform prolonged load-bearing activities, with full-duty loads in excess of 50 to 100 lb and frequent exposure to uneven terrain and austere conditions. We hypothesized that OCA would reliably restore the majority of military servicemembers to preoperative occupational function with lower rates of secondary revision or short-term to midterm surgical failure.

METHODS

After obtaining approval from the local institutional review board, a retrospective review of the Management Analysis and Reporting Tool (M2) database within the United States Military Health System was performed to identify all active-duty servicemembers who underwent OCA (Current Procedural Technology codes 27415 and 29867) between January 2009 and March 2013. Inclusion criteria included active-duty US Army servicemembers with a minimum 2-year follow-up and confirmed treatment of OCA for a medium to large osteochondral lesion (>2 cm^2). Exclusion criteria consisted of nonmilitary beneficiaries (eg, family members, retirees, Veterans Affairs beneficiaries), other branches of military service (navy, air force, marines), insufficient follow-up period, inadequate health record documentation, and procedure miscoding (eg, particulated juvenile allograft transplantation).

Demographic data that were recorded included age, sex, race, branch of service, insurance beneficiary status, and date of service. Rank was defined as junior enlisted (E1-E4), senior enlisted (E5 and above), and officer (including chief warrant officers). Patients were subsequently cross-referenced with the military electronic medical record (Armed Forces Health Longitudinal Technology Application [AHLTA]), and an independent chart review was performed to confirm the presence of an index OCA procedure. After identification, additional demographic data were obtained from the electronic health record to include current military rank, body mass index (BMI), and tobacco use. Clinical data were also extracted, including lesion location, size of the allograft used, prior procedures, preoperative and postoperative (final follow-up) visual analog scale (VAS) for pain scores, concurrent or staged procedures (eg, high tibial osteotomy), and clinical course. The independent variables examined for an association with the final outcomes included sex, age, lesion location, lesion size, preoperative BMI, tobacco use, preoperative VAS score, postoperative VAS score, presence of a perioperative complication, and subsequent ipsilateral knee procedure. VAS scores were subdivided into mild (score <4) or moderate to severe pain (score $\geq$4).

Overall failure was subdivided according to clinical failure, defined as the inability to return to modified military activities because of persistent knee dysfunction or medical separation from the military (Medical Evaluation Board [MEB]), or surgical failure, defined as a revision chondral or osteochondral procedure and/or subsequent arthroplasty. We did not track separation data for patients who lacked a 2-year follow-up. A revision cartilage procedure was defined as secondary osteochondral transplantation, marrow stimulation, ACI, or other repair or reconstructive techniques at the site of the index OCA. For the purposes of this study, the rate of subsequent graft debridement or chondroplasty was recorded; however, this was not considered a failure or revision procedure, as it did not necessitate a full rehabilitation course associated with other chondral restoration procedures. Complications included infections, fractures, and arthrofibrosis; subsequent graft-specific and/

[§]Address correspondence to Brian R. Waterman, MD, Department of Orthopaedic Surgery, Wake Forest Baptist Medical Center, 1 Medical Center Boulevard, Winston-Salem, NC 27157, USA (email: brian.r.waterman@gmail.com).

*Department of Surgery, Munson Army Health Center, Fort Leavenworth, Kansas, USA.

[†]Department of Orthopaedic Surgery, Dwight D. Eisenhower Army Medical Center, Fort Gordon, Georgia, USA.

[‡]Department of Orthopaedic Surgery, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, USA.

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Ethical approval for this study was obtained from the Dwight D. Eisenhower Army Medical Center Institutional Review Board.

TABLE 1
Demographics of Patients (N = 61)

	Mean ± SD or n (%)
Age, y	31.7 ± 8.0
Age group	
<31 y	28 (45.9)
≥31 y	33 (54.1)
Sex	
Male	52 (85.2)
Female	9 (14.8)
Body mass index	
<30 kg/m^2	43 (70.5)
≥30 kg/m^2	18 (29.5)
Rank	
Junior enlisted	19 (31.1)
Senior enlisted	31 (50.8)
Officer/chief warrant officer	11 (18.0)
Race	
White	30 (49.2)
Black	16 (26.2)
Asian	2 (3.3)
Unknown	13 (21.3)
Tobacco use	
Yes	20 (32.8)
No	41 (67.2)
Follow-up, mo	46.2 ± 14.5

or complication-related procedures were also recorded. Hardware removal was not considered a complication or unplanned reoperation in this series, as some patients were counseled preoperatively about the potential for secondary hardware removal if prominent or localized symptoms persisted.[32]

Statistical Analysis

Data analysis was performed using the SPSS statistical package (version 24; IBM). Significance was set at $P < .05$. Descriptive statistics were generated. Univariate analysis was performed to assess for associations between the identified variables with either clinical or surgical failure. Cutoff values for variables were selected, when appropriate, from statistical analysis. Furthermore, bivariate analysis was performed to see which variables were associated with any type of failure. The relative risk was quantified through the use of odds ratios (ORs) with 95% CIs.

RESULTS

Demographics

Overall, 763 patients were coded using the procedural codes of interest. Of these, 648 were excluded (353 were non-army personnel, 241 lacked a minimum 2-year follow-up, 54 were excluded for miscellaneous issues, and 54 were coded incorrectly), leaving 61 patients (52 male, 9 female) eligible for consideration (Table 1). The mean patient age was 31.7 ± 8.0 years, and patients had a mean follow-up of 46.2 months. Senior enlisted personnel made up the majority of the cohort; 41 patients (67.2%) did not use nicotine or tobacco products of any kind.

TABLE 2
Anatomic Location of Lesions[a]

	Overall, n (%)	Mean Size, mm^2	Revision, n (%)	Clinical Failure, n (%)
MFC	40 (63.5)	364	4 (10.0)	13 (32.5)
LFC	8 (12.7)	328	2 (25.0)	4 (50.0)
Patella	12 (19.0)	325	1 (8.3)	4 (33.3)
Trochlea	3 (4.8)	700	1 (33.3)	1 (33.3)
Total	63	365	8	22

[a]LFC, lateral femoral condyle; MFC, medial femoral condyle.

Surgical Variables

A total of 63 lesions were identified in 61 knees. The most common location was the medial femoral condyle (MFC) (n = 40; 63.5%), followed by the patella (n = 12; 19.0%), lateral femoral condyle (n = 8; 12.7%), and trochlea (n = 3; 4.8%) (Table 2). Two knees had multiple lesions, including 1 with defects of the MFC and trochlea and another with bipolar lesions of the patella and trochlea. The majority of knees (n = 39; 63.9%) had undergone ≥1 prior procedures, with only 22 (36.1%) being performed as an index procedure (not inclusive of prior staged arthroscopic surgery). A total of 58 prior therapeutic procedures had been performed, with the most common being microfracture, unrelated to the primary OCA (n = 19; 32.8%), followed by chondroplasty (n = 12; 20.7%). Open OCA was performed in isolation for the majority of patients (n = 37; 60.7%), but a total of 33 concomitant procedures were performed in 24 patients. The most common concomitant procedures were off-loading tibial tubercle osteotomy (n = 10) and high tibial osteotomy (n = 10; 16.4%) (Table 3).

Surgical Outcomes and Complications

The mean postoperative VAS pain score at final follow-up was 2.68 ± 2.73, an improvement by a mean of 1.42 ± 3.06 from 4.10 ± 2.17 preoperatively, which was statistically significant ($P < .0009$). Episodic joint line pain was present in 34 patients (55.7%) postoperatively. Of the patients with continued pain, 25 (41.0% of the total cohort) could be rated as moderate to severe, as defined by a VAS score ≥4. There were 6 surgical failures requiring revision (9.8%). Five complications (8.2%) were identified, including 1 stress fracture (due to tibial tubercle osteotomy) that was managed nonoperatively, 2 cases of arthrofibrosis requiring arthroscopic lysis of adhesions, and 2 infections requiring intravenous antibiotics and surgical debridement (Table 4).

Revision and Secondary Surgery

There were 17 patients (27.9%) who required a total of 23 subsequent procedures. In 2 patients, the subsequent

TABLE 3
Additional Procedures Performed[a]

	Prior	Concurrent	Subsequent	Total
Meniscal procedures				
Debridement	4	0	1	5
Repair	2	1	0	3
Transplantation	1	2	0	3
Ligamentous procedures				
Anterior cruciate ligament repair	3	1	0	4
Posterior cruciate ligament repair	0	1	0	1
Medial collateral ligament repair	0	0	1	1
Lateral release	0	4	1	5
Osteotomy				
High tibial osteotomy	3	10	0	13
Distal femoral osteotomy	0	1	0	1
Tibial tubercle osteotomy	0	10	0	10
Cartilage procedures				
Chondroplasty	12	0	5	17
ORIF for osteochondritis dissecans	4	0	0	4
Microfracture	19	3	0	22
OAT	5	0	0	5
OCA	0	0	4	4
ACI	2	0	1	3
Arthroplasty	0	0	1	1
Lysis of adhesions	0	0	2	2
Hardware removal	0	0	5	5
Irrigation and debridement	0	0	2	2
Other[b]	3	0	0	3
Total	58	33	23	

[a]Data are reported as No. Procedures are listed according to type and timing of surgery relative to OCA. ACI, autologous chondrocyte implantation; OAT, osteochondral autograft transfer; OCA, osteochondral allograft transplantation; ORIF, open reduction internal fixation.

[b]Anterior interval release, medial collateral ligament repair, and scar revision.

TABLE 4
Outcomes and Complications[a]

	n (%)
Surgical outcomes	
Persistent pain	34 (55.7)
Revision cartilage procedure	5 (8.2)
Total knee arthroplasty	1 (1.6)
Clinical outcomes	
MEB	22 (36.1)
Return to duty	39 (63.9)
Overall outcomes	
Return to duty without revision	35 (57.4)
Total failure	26 (42.6)
Complications	
Infection	2 (3.3)
Arthrofibrosis	2 (3.3)
Fracture	1 (1.6)

[a]MEB, Medical Evaluation Board for separation from military.

procedures were unrelated to the initial cartilage surgery (lateral release and medial collateral ligament repair). Five patients required 6 revision cartilage procedures (revision OCA: n = 4 [6.6%]; revision ACI, n = 1 [1.6%]), with 1 patient undergoing 2 secondary procedures and 1 patient (combined MFC and trochlear lesions) being converted to total knee arthroplasty (Table 4). Secondary chondroplasty or graft debridement was performed in 5 patients (8.2%) for partial graft delamination. In the 2 patients with multiple lesions, both were able to resume occupational function postoperatively with continued military service. However, the patient with MFC and trochlear lesions required conversion to total knee arthroplasty for persistent medial pain. The patient with bipolar patellofemoral lesions did not require any subsequent procedures.

Clinical Outcomes

A total of 22 patients (36.1%) were unable to return to modified preoperative function because of persistent, rate-limiting knee pain after OCA, while 39 (63.9%) were able to return to preoperative military function. Of the patients who underwent revision cartilage procedures, 3 of the 5 (60.0%) were able to return to military duty, and the 1 patient who underwent subsequent arthroplasty was also able to resume military service with permanent limitations on impact activities. Accordingly, the overall failure rate, as defined in this study, was 42.6% (n = 26).

Risk Factor Analysis

Risk factors for clinical failure on logistic regression analysis were found to be preoperative BMI, preoperative VAS score, and moderate to severe postoperative pain (VAS score ≥4) (Table 5), whereas the only significant risk factor for surgical failure was the presence of a complication. Risk factors for overall failure were found to be the presence of ≥1 complications (OR, 7.33) and moderate to severe postoperative pain on the VAS (OR, 9.92). Lesion size and lesion location were not found to be factors in contributing to either surgical or clinical failure. Rank was not found to be a risk factor for failure of OCA. Osteotomy and any prior procedure, specifically including prior chondral treatments, also were not found to contribute to either mode of failure.

DISCUSSION

In this series of active-duty army servicemembers, representing the largest cohort to date of OCA performed on military personnel, OCA was found to reduce knee pain associated with medium to large osteochondral lesions and to afford a return to preoperative military function in approximately 64% of patients. Overall, revision surgery occurred in 8.2%, and 1.6% underwent conversion to knee arthroplasty at short-term to midterm follow-up. Furthermore, moderate and higher postoperative VAS pain scores and the presence of a perioperative complication were identified as significant risk factors for overall failure, defined

TABLE 5
Risk Factors for Failure[a]

	Clinical Failure		Surgical Failure		Overall Failure	
	OR	*P*	OR	*P*	OR	*P*
Total lesion size	1	.474	1	.999	1	.748
Preoperative body mass index	**1.18**	**.029**	0.75	.054	1.07	.322
Tobacco use	1.29	.655	4.88	.083	1.56	.417
Preoperative VAS score	**1.32**	**.043**	1.06	.779	1.28	.054
Moderate to severe postoperative pain on VAS	**1.36**	**.007**	18.52	.056	**9.92**	**.0002**
Lesion location						
MFC	0.64	.425	1.06	.95	0.73	.568
LFC	1.94	.384	4.08	.146	2.54	.234
Patella	0.86	.826	0.27	.398	0.61	.470
Trochlea	0.88	.920	5.30	.203	2.83	.406
≥1 complications	1.22	.777	**148.76**	**.002**	**7.33**	**.018**
Age <31 y	0.73	.557	6.96	.086	1.02	.973
Female sex	2.57	.197	0.38	.538	1.85	.400
Any prior surgery	1.86	.286	3.09	.318	2.81	.073
Any prior chondral surgery	2.14	.160	0.65	.630	2.24	.129
Osteotomy	1.14	.811	0.35	.353	0.75	.605

[a]Bolded data indicate statistical significance ($P < .05$). LFC, lateral femoral condyle; MFC, medial femoral condyle; OR, odds ratio; VAS, visual analog scale.

as either the requirement for revision surgery or knee-related medical discharge.

The management of persistently symptomatic chondral defects among young, active patients is problematic. The optimal solution for this problem has not yet been elucidated. While technically easier and readily available as a single-staged procedure, the efficacy and long-term durability of microfracture have often been called into question, especially with larger lesions.[8,26] Studies in National Basketball Association (NBA) players have shown that patients who underwent microfracture were at significant risk of not returning to competitive play, while those who did resume elite competition had a significant reduction in points per game.[5,13] Conversely, in a systematic review, OAT has shown more enduring results at long-term follow-up.[31] In a meta-analysis of available techniques for chondral repair or restoration, OAT was associated with the highest rates of return to sport, followed by OCA and ACI, respectively.[17] Unlike other techniques, the success of OAT may be attributable to its use of mature, organized, autogenous articular cartilage as well its general use for smaller, focal lesions versus that for more mosaicplasty applications.[3]

The role of subchondral bone in the setting of chondral defects should not be minimized.[21] Minas et al[23,24] showed that despite favorable results at 10-year follow-up after ACI, a subset of patients with worse outcomes had undergone a prior marrow stimulation procedure, which resulted in a compromised subchondral bone architecture. OCA has been found to be effective in the setting of prior marrow stimulation and other prior chondral procedures because of the transplant of the entire osteochondral unit as a whole.[9-11] In a large case series report by Sadr et al,[34] OCA was found to be a very effective treatment modality for osteochondritis dissecans lesions that had failed other treatment strategies. OAT also affords for the transfer of a mature construct but is constrained by lesion size, matching of the radius of curvature, limited availability of harvest sites, and incomplete treatment with the mosaicplasty technique in larger lesions up to 4 cm^2.[20,25,27] Alternatively, the use of a fresh, size-matched osteochondral allograft obviates these constraints and allows complete reconstitution of the surrounding osteoarticular anatomy.

OCA has been proven to be very effective at alleviating pain, mechanical symptoms, and symptomatic effusion while restoring function for lower demand activities.[1,2,12] Few studies have investigated the outcomes of OCA in active, athletic patient subsets.[37] At 2.5-year follow-up, Krych et al[18] reported that 88% of 43 athletes (74% recreational, 26% competitive) returned to limited sporting activities, with 79% achieving a full return to preinjury levels. In the group that achieved full return to sport, the average time to full sporting activity was 9.6 months. Nielsen et al[29] recently showed that at 6-year follow-up, just over 75% of patients who underwent OCA were still participating at their preoperative level of sport, both recreational and competitive. By contrast, cell-based surface treatments that use an immature chondral construct may delay a return to impact sporting activities for up to 12 to 18 months postoperatively, and the implanted cartilage may continue to develop its mature architecture over another 12 to 18 months,[15,28] although other reports have found conflicting results and improved return-to-sport rates.[16] Additionally, although Pestka et al[33] showed that 73% of patients undergoing ACI returned to sport, in-depth analysis indicated that high-impact and start-stop activities were typically exchanged for endurance and low-impact activities. An elite level of sporting activities was maintained in less than 1% of the patient population.

The current study is one of the few assessing functional outcomes among higher demand patients with significant occupational requirements. Unlike the results shown by Krych et al[18] and Nielsen et al,[29] the return to high-demand lower extremity functionality among military patients was more variable, with moderate success at returning patients to preoperative occupational activities. Despite a smaller sample size, the demands placed on army servicemembers put them at a level beyond a purely recreational athletic level, and this may explain the disparity in and definitions for postoperative "success." Servicemembers are often required to perform prolonged load-bearing activities, with full-duty loads in excess of 50 to 100 lb and frequent exposure to uneven terrain and austere conditions. Scully et al[35] showed that in 16 patients undergoing OCA performed at a single military institution, 9 (56.3%) underwent medical separation from the military (MEB) within 24 months, and of the remaining 7 patients, 6 (37.5% of total) required significant activity limitation. Another military study by Shaha et al[36] yielded somewhat similar results to the present study, with 16 of 38 (42.1%) servicemembers who underwent OCA being unable to return to military duty. This is almost identical to our overall failure rate (42.6%) and very similar to our clinical failure rate (36.1%). However, it is important not to conflate surgical failure with knee-related medical separation, as many military servicemembers may experience successful functional outcomes in a civilian environment with more limited daily occupational demands.

Chronological age is a factor that is commonly thought to affect clinical outcomes after cartilage procedures. Zarkadis et al[41] demonstrated comparatively worse outcomes in patients younger than 30 years undergoing ACI for patellofemoral lesions. Particularly in the military population, this is thought to be related to the preponderance of younger servicemembers holding junior enlisted rank positions. These servicemembers often lack individual autonomy or the ability to self-regulate their activity levels upon return to duty. Conversely, older patients tend to be officers or senior enlisted personnel who are given more authority to dictate their level of physical activities. In the current study, we did not find a significant effect for age and the rate of failure. We also did not find any trends in failure according to lesion location. Traditional difficult-to-treat areas, such as the patella and trochlea, have shown good outcomes in previous studies when treated with OCA.[4,10] A revision chondral procedure or conversion to arthroplasty did not guarantee that the servicemember would need a medical discharge due to his/her knee defect. The need for osteotomy also did not, by itself, portend a poor outcome. The fact that there was no difference in outcomes between those who did and did not undergo osteotomy does not lend itself to the conclusion that osteotomy itself is an unnecessary procedure. Rather, osteotomy removes malalignment (with the resultant abnormal loading forces) as a source of failure and thus essentially places all the chondral lesions in an equivalent biomechanical environment.

Despite its modest size, this study features numerous strengths. The military framework provides a closed health care setting that is ideal for the surveillance of musculoskeletal conditions because of a centralized electronic medical record and injury reporting system. Additionally, the high-demand physical profile of military servicemembers and the underlying emphasis on physical fitness standards and military readiness may translate well to other physically active patient populations, particularly athletes and those involved in heavy-labor occupations. However, certain limitations must also be acknowledged. Because of the scope and retrospective nature of this investigation, surgical technique, technical proficiency, and rehabilitation course could not be controlled for. Radiographic studies were not available to further evaluate and classify lesions. Furthermore, additional validated patient-reported outcome measures and advanced radiographic imaging confirming graft incorporation were not routinely available in the medical record.

Additionally, graft processing technique is an important consideration but one that we were unable to account for in the present study. Several patients had multiple cartilage lesions, which may have limited the effectiveness of OCA. The lack of patient-reported outcomes, which cannot be easily extrapolated from military separation data, is also a point of contention. Additionally, we did not have separation data on patients who were lacking 2-year follow-up, so it is possible that some patients who separated early from the military because of their knee symptoms were not captured. Last, while we sought to objectively identify patients with persistent knee symptoms that precluded a return to preoperative military function, we cannot exclude the potential for secondary gain motivations in pursuing permanent activity limitation or physician-directed medical discharge to prevent further reinjuries.

CONCLUSION

Approximately two-thirds of active-duty military servicemembers undergoing OCA were able to return to preinjury occupational activities. Moderate to severe postoperative pain and the presence of a complication were risk factors for overall failure. Patients should be counseled preoperatively regarding expectation management and should be aware that although pain is likely to improve, certain permanent activity restrictions may exist.

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