Autologous Chondrocyte Implantation and Tibial Tubercle Osteotomy for Patellofemoral Chondral Defects

Improved Pain Relief and Occupational Outcomes Among US Army Servicemembers

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Background: The occupational and functional results of patellofemoral autologous chondrocyte implantation (ACI) are underreported. This investigation sought to establish clinical outcomes and rates for return to work in a predominantly high-demand military cohort undergoing this procedure.

Purpose: To determine the return-to-work, pain relief, and perioperative complication rates in a high-demand athletic cohort undergoing patellofemoral ACI.

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

Methods: All military servicemembers from 2 military medical centers undergoing ACI for high-grade patellofemoral chondral defects between 2006 and 2014 were identified, and data were abstracted from their medical records and clinical databases. Demographic and surgical variables were obtained for patients with at least 2 years of postoperative follow-up, and perioperative complications, rates of return to work, and survivorship from revision were quantified.

Results: Seventy-two patients (72%) had >2-year follow-up and had patellofemoral ACI for high-grade chondral defects, with 66 knees (91%) undergoing a concomitant offloading tibial tubercle osteotomy. Mean follow-up was 4.3 years (range, 2.0-9.9 years). The mean ± SD age was 34.4 ± 6.1 years; 86% were male; and 57% were involved in military occupational specialties of heavy or very heavy demand. Second-generation patellofemoral ACI with a type I/III collagen membrane was used for 85% of knees. Most defects were isolated to the patella (n = 40, 55%). The mean total defect surface area was 4.5 ± 2.9 cm^2 (range, 2.7-13.5 cm^2). Fifty-six servicemembers (78%) returned to their occupational specialties. Three patients (4.1%) were classified as having surgical failures, requiring subsequent knee arthroplasty (n = 2) or a revision chondral procedure (n = 1). Mean visual analog scores improved significantly from 6.5 ± 1.5 to 3.2 ± 2.1 ($P < .0001$). Multivariate analysis identified use of a periosteal patch as the only significant independent predictor for surgical ($P = .013$) and overall ($P = .033$) failures. Age <30 years ($P = .019$), female sex ($P = .019$), and regular tobacco use ($P = .011$) were independent predictors of overall failure.

Conclusion: For patellofemoral chondral defects without a failed primary procedure, second-generation ACI successfully returned to work 78% of patients of moderate to very heavy occupational demand with significantly decreased patient-reported knee pain. Risk factors after ACI for patellofemoral articular lesions for overall failure were age <30 years, female sex, and tobacco use, while surgical and overall failures were associated with periosteal patch use.

Keywords: autologous chondrocyte implantation; patellofemoral; military; knee; articular cartilage

Anterior knee pain attributed to isolated patellofemoral chondromalacia is common, with a reported prevalence of 15% to 20% among symptomatic patients evaluated by magnetic resonance imaging.[59] If left untreated, focal articular cartilage defects of the knee can cause significant pain and disability and ultimately progress to degenerative arthritis. There is a strong correlation between knee pain with patellofemoral arthritis and ensuing functional limitation.[10,11,29,61,63] Prior reports identified increased baseline levels of physical activity as a significant risk factor

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for the development of knee osteoarthritis.[53,58,65] Similar findings were observed in the military and are among the primary causes of medical disability and resultant military discharge among servicemembers.[8,46,55,57]

While there are many treatment options for patellofemoral cartilage defects, each should be tailored to the functional demands of the patient. Management may differ depending on lesion size, compartment location, knee alignment, meniscal integrity, and ligament status. Within the patellofemoral articulation, there are various surgical treatment options, and these can be broadly categorized as palliative (eg, chondroplasty), reparative (eg, microfracture and subchondral drilling), and restorative (eg, osteochondral autograft transfer, autologous chondrocyte implantation [ACI], and osteochondral allograft transplantation).[35]

First introduced as a restorative treatment option in 1994, ACI allows for incorporation of a hyaline-like cartilage with reproducible longevity and wear characteristics up to 20 years after implantation.[6,20,49] Furthermore, ACI has been shown to reduce pain in young active populations and improve knee function, with a return to preinjury activity for 73% to 84%.[7,47] These findings make ACI an appealing alternative for the early treatment of military servicemembers diagnosed with degenerative and posttraumatic knee osteoarthritis.[57] However, reported outcomes of ACI in the patellofemoral articulation are less reliable, and its use for patellar chondral lesions was off-label according to the US Food and Drug Administration until 2017.

ACI, particularly involving the patellofemoral joint, has not been thoroughly evaluated among younger, physically active military servicemembers. The purpose of this investigation was to determine the return-to-work, pain relief, and perioperative complication rates in a high-demand athletic cohort undergoing patellofemoral ACI with a minimum 2-year occupational follow-up. We hypothesized that patellofemoral ACI coupled with offloading tibial tubercle osteotomy (TTO) would reliably decrease anterior knee pain and facilitate a predictable rate of return to lower extremity function.

METHODS

Patient Population

After institutional review board approval, all patients undergoing patellofemoral ACI (Current Procedural Terminology code 27412) for a high-grade patellofemoral chondral defect between February 2006 and December 2014 at 2 military medical centers were identified by utilizing the military surgical scheduling system. Exclusion criteria were applied to individuals with <2 years of clinical follow-up, nonmilitary or retired status at the time of surgery, ACI procedures performed outside the patellofemoral joint, and/or those with insufficient documentation (Figure 1).

Demographics and Surgical Characteristics

The US Department of Defense electronic health record, Armed Forces Health Longitudinal Application (v 3.3), was examined to verify the accuracy of the Current Procedural Terminology coding and to record the age, sex, body mass index, tobacco use, military rank, branch of service, military occupational specialty, surgical indications, prior ipsilateral knee surgery, preoperative patellar instability events, and clinical course. Radiologic and surgical characteristics collected included the tibial tubercle–trochlear groove distance,[56] patellofemoral chondral defect size and location, Outerbridge score,[44] concomitant surgical procedures, perioperative complications, and secondary surgical procedures. The rank groups were categorized as junior rank (junior enlisted soldiers, E1-E5), senior rank (senior enlisted noncommissioned officers, E6-E9), or officers and civilians (warrant officers, WO1-WO5; commissioned officers, O1-O6). The military occupational specialty designations were classified as combat arms, combat support, or combat service support based on inherent occupational demands.

Surgical Technique

During the stage I ACI procedure, the operative surgeon harvested a 250- to 300-mg full-thickness chondral biopsy specimen from the nonweightbearing and nonarticulating portion of the intercondylar femoral notch. The chondral specimens were sent to the laboratory for culture and chondrocyte expansion. A stage II ACI procedure was performed with 1 of 2 surgical techniques: first-generation ACI with a periosteal patch[37] or second-generation ACI with a type I/III collagen membrane (Vericel Inc).[60] Concomitant procedures at the time of stage II ACI were identified to include TTO, lateral retinacular lengthening, and medial patellofemoral ligament reconstruction.

For the TTO, a centrally based skin incision was performed with a medial parapatellar approach. The patella was delivered with small elevation of the prepatellar fat pad to allow mobilization. The proximal anterior

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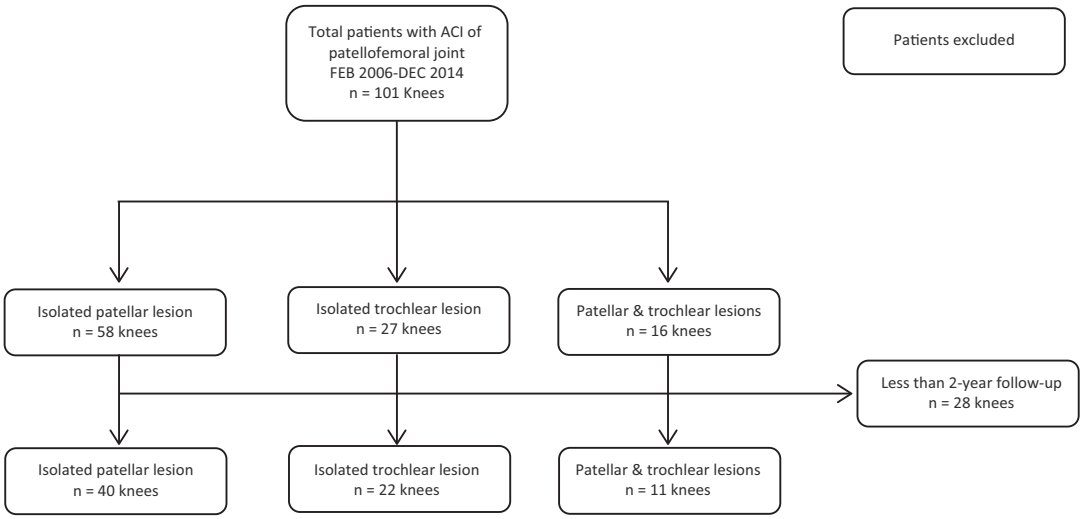

Figure 1. Primary autologous chondrocyte implantation (ACI) patient selection diagram for patellofemoral articular cartilage defects.

compartment of the leg was then gently elevated from the proximal anterolateral tibia. A tibial tubercle cut 45° to 60° was then made measuring 6 to 8 cm long. After ACI, the TTO was then fixed to its new position with 2 or 3 bicortical screws in a lag-by-technique fashion.

At this point in time, the patella was everted; a moist Ray-Tec was placed around the tibial tubercle osteotomy; and the cartilage surfaces were evaluated. The cartilage defect was measured, and all diseased cartilage tissue was demarcated with a knife. Afterward, a curette was utilized to obtain vertical margins and healthy cartilage encompassing the defect.

Postoperative Rehabilitation

The patients were initially prescribed a hinged knee brace locked in full extension and were nonweightbearing during the first 2 weeks postoperatively. Range of motion was controlled with a continuous passive motion machine for the first 3 weeks, starting on postoperative day 1 (0°-30° at 1 cycle/min, 6-8 h/d). Range of motion was then advanced at 5° to 10° per day with a goal of 90° by week 6 and 120° by week 8 with discontinuation of the continuous passive motion machine. Partial weightbearing began at 2 weeks and progressed to weightbearing as tolerated beginning at 6 weeks. If TTO was performed concomitantly, the patient was kept nonweightbearing until 6 weeks postoperatively. Low-impact aerobic activities and plyometric exercises were allowed at 6 months. Running was restricted until the 1-year mark. Return to unrestricted activities was permitted at 18 months postoperatively if the patient was pain-free with activity.

Outcomes

The primary outcomes of interest were (1) occupational outcome failure, defined as an inability to return to military duty service or previous civilian occupation after ACI because of persistent knee pain or symptomatology; and (2) surgical failure, constituting a revision chondral procedure or conversion to arthroplasty. In accordance with previous studies,[4,33] definitions from the US Department of Labor's *Dictionary of Occupational Titles*[9] were used to assess physical job demand categories: sedentary, light, medium, heavy, and very heavy. Overall failure was defined as meeting the criteria for occupational outcome failure and/or surgical failure. The occupational requirements of military servicemembers are described in detail within the standards of medical fitness for the Air Force, Army, and Navy.[1,2,36] The military occupational specialty designations were categorized in accordance with the US Department of Labor's *Dictionary of Occupational Titles* for preoperative physical job demand categorization: heavy/very heavy, combat arm and combat support MOS (military occupational specialty); medium, combat service support; light, civilian. The Physical Profile (DA 3349) within the e-Profile electronic profiling system (v 3.17; Medical Operational Data System) was used to record all physical duty limitations and final medical separations. All military servicemembers in the cohort undergoing ACI for high-grade patellofemoral chondral defect and initiation of a knee-related medical separation after ACI were identified and cross-referenced with the US Army Physical Disability Agency Database, the electronic medical record, and/or the e-Profile system. Additional outcomes included changes in visual analog scale (VAS) scores and performance of a combat deployment after ACI. The VAS is a verbal subjective pain value reported on a 0-10 scale, and this value is recorded at each patient visit. Previous studies defined an improvement of 2 points or a 30% reduction in the VAS score as a clinically important difference.[13,15,50] The Pentagon Defense Manpower Data Center ascertained combat deployments.

Statistical Analysis

Univariate logistic regression analysis was performed to test the significance of demographic, injury-related, and

TABLE 1
Patient Characteristics and Clinical Profile[a]

	n (%) or Mean ± SD
Patients	72
Knees	73
Follow-up, y	4.3 ± 2.0
Age, y	34.4 ± 6.1
Men	63 (86)
Women	10 (14)
Tobacco use	32 (44)
Body mass index, kg/m^2	28.1 ± 3.6
Service	
Army	66 (91)
Navy	1 (1)
Air Force	6 (8)
Rank	
Junior enlisted	12 (16)
Senior enlisted	46 (63)
Officer	15 (21)
MOS	
Combat arms	17 (23)
Combat support	25 (34)
Combat service support	31 (43)

[a]Percentages were calculated per the number of knees (n = 73). MOS, military occupational specialty (eg, profession).

TABLE 2
Patellofemoral Articular Cartilage Injury Characteristics[a]

	n (%) or Mean ± SD
Number of defects by location	
Isolated patellar lesion	40 (55)
Isolated trochlear lesion	22 (30)
Bipolar patellofemoral lesions[b]	11 (15)
Outerbridge grade	
Patellar lesion	3.9 ± 0.3
Trochlear lesion	3.7 ± 0.5
Total defect surface area, cm^2	
≥6	20 (28)
4-5.9	19 (26)
2-3.9	22 (30)
<2	12 (16)
Defect surface area, cm^2	
Total lesion	4.5 ± 2.9
Patellar lesion	4.3 ± 2.2
Trochlear lesion	3.4 ± 2.0
TT-TG distance, mm	12.9 ± 3.6
≥20	3 (6)
15-19.9	10 (21)
10-14.9	22 (47)
<10	12 (26)

[a]Percentages were calculated per the number of knees (n = 73). TT-TG, tibial tubercle–trochlear groove.
[b]Bipolar patellofemoral lesions represent lesions present on the articular surface of the patella and trochlea.

surgical risk factors as predictors of clinical, surgical, and overall failure. Multivariate regression analysis was subsequently performed for any risk factors with P values <.05 on initial univariate analysis, and significant independent predictors were defined as those with P values <.05 and 95% CI for the odds ratio (OR) exclusive of 1.0. All statistical calculations were performed with SAS (v 9.4; SAS Institute Inc). A paired t test was used to compare pre- versus postoperative changes in VAS score for all knees and those that would be classified as occupational outcome failures and surgical failures.

RESULTS

Demographics

A total of 72 active duty military service members (73 knees) met inclusion criteria (Table 1). The mean ± SD age of the patients at the time of surgery was 34.4 ± 6.1 years (range, 20-50 years), while the mean body mass index was 28.1 ± 3.6 kg/m^2. Most patients were male (86%), army servicemembers (91%), and of senior enlisted rank (63%). The mean follow-up from time of surgery was 4.3 years (range, 2.0-9.9 years).

Surgical Variables

The majority of cartilage defects were unipolar (85%), isolated to the patella (55%), and >4.0 cm^2 (54%) and most knees had a mean tibial tubercle–trochlear groove distance <15 mm (73%) (Table 2). The mean Outerbridge grades for the patella and trochlea were 3.9 ± 0.3 and 3.7 ± 0.5, respectively. The mean defect sizes for the patella and trochlea were 4.3 ± 2.2 cm^2 (range, 1.7-13.5 cm^2) and 3.4 ± 2.0 cm^2 (range, 1.0-9.0 cm^2), respectively.

Most patients had had at least 1 ipsilateral knee surgical procedure before ACI (n = 42, 58%), with 12 patients undergoing >1 previous surgical procedure (Table 3). Abrasion chondroplasty accounted for >60% of the previous surgical procedures performed (n = 25). There were 69 concomitant surgical procedures performed among 66 patients. TTO procedures were concurrently performed with ACI in 66 knees (91%). The indications for all concurrent TTOs included distal (n = 18) and lateral (n = 26) patellar chondral defects, lateral trochlear defects (n = 7), combined patellar instability (n = 4), and/or tibial tubercle–trochlear groove >15 mm (n = 15). Four patients had >1 indication for TTO. Concomitant medial patellofemoral ligament (n = 1) and lateral retinacular lengthening (n = 2) procedures were performed in cases of patellar instability. Sixty-two knees (85%) had a second-generation ACI with a type I/III collagen membrane, and 11 knees (15%) had a first-generation ACI with a periosteal patch for the second stage of ACI.

Outcomes

At a minimum occupational follow-up period of 2 years postoperatively, 56 servicemembers (78%) returned to their medium to very heavy occupational demand categories of active duty service or fulfilled their remaining service obligations (Table 4). A total of 16 servicemembers

TABLE 3
Prior and Concomitant Knee Procedures[a]

	n (%)
Any knee surgery before ACI	42 (58)
Chondroplasty	25 (34)
Microfracture	9 (12)
Meniscal debridement	9 (12)
Lateral release	8 (11)
Anterior cruciate ligament reconstruction	5 (7)
Meniscal repair	3 (4)
Previous medial patellofemoral ligament reconstruction	1 (1)
Any concomitant knee surgery during ACI	66 (91)
Tibial tubercle osteotomy	66 (91)
Lateral retinacular lengthening	2 (3)
Medial patellofemoral ligament reconstruction	1 (1)
ACI technique	
Periosteal patch	11 (15)
Type I/III collagen membrane	62 (85)

[a]Percentages were calculated per the number of knees (n = 73). ACI, autologous chondrocyte implantation.

(22%) were medically separated secondary to persistent, rate-limiting knee symptoms. Among the 72 servicemembers, 29% (n = 21) performed a combat deployment after the ACI procedure. At final follow-up, 3 patients (4.2%) were qualified as having surgical failures; 2 required conversion to patellofemoral arthroplasty; and revision chondral surgery was performed for 1 patient. The cases of 17 patients (24%) were classified as overall failures, as 2 met criteria for both occupational outcome failure and surgical failure. The mean VAS pain score demonstrated a significant improvement from 6.5 ± 1.5 (range, 3-10) at baseline to 3.2 ± 2.1 (range, 0-9) postoperatively ($P < .0001$) (Figure 2). Additionally, the occupational outcome failure and surgical failure subgroups had significant improvement in VAS pain scores ($P < .05$).

Complications

Among the 73 knees undergoing patellofemoral ACI for a high-grade patellofemoral chondral defect, 29 complications occurred among 26 patients: symptomatic hardware removal from the TTO (16%, n = 12), second-look diagnostic arthroscopy for pain (8%, n = 6), periosteal graft hypertrophy requiring surgical debridement (5%, n = 4), arthrofibrosis requiring manipulation under anesthesia (5%, n = 4), arthroscopic meniscal debridement (1%, n = 1), open reduction and internal fixation for fracture around the TTO (1%, n = 1), and full-thickness wound dehiscence requiring irrigation and debridement (1%, n = 1). The 6 patients who underwent second-look diagnostic arthroscopy reported continued knee pain with benign examination and normal diagnostic imaging results. There was no evidence of graft delamination or hypertrophy at the time of second-look arthroscopy among patients with persistent pain. All ACI-treated cartilage defects demonstrated complete incorporation of the regenerate cartilage, and no other intra-articular source of pain was identified at

TABLE 4
Outcomes and Complications After ACI[a]

	n (%)
Occupational outcome failure based on preoperative physical job demand categorization	
Heavy/very heavy	6
Medium	10
Light	0
Total	16 (22)
Surgical failure based on preoperative physical job demand categorization	
Heavy/very heavy	3
Medium	0
Light	0
Total	3 (4)
Overall failures	17 (24)[b]
Combat deployment after ACI	21 (29)
Complications[c]	
Removal of hardware	12 (16)
Arthroscopy for pain	6 (8)
Periosteal graft hypertrophy	4 (6)
Manipulation under anesthesia	4 (6)
ORIF	1 (1)
Irrigation and debridement	1 (1)
Meniscal debridement	1 (1)

[a]Percentages were calculated per the number of servicemembers (n = 72) unless noted otherwise. ACI, autologous chondrocyte implantation; ORIF, open reduction internal fixation.
[b]Two patients underwent conversion to patellofemoral arthroplasty, and 1 underwent a revision chondral procedure. Two patients met criteria for both occupational outcome and surgical failures.
[c]Complication percentages were calculated per the number of knees (n = 73).

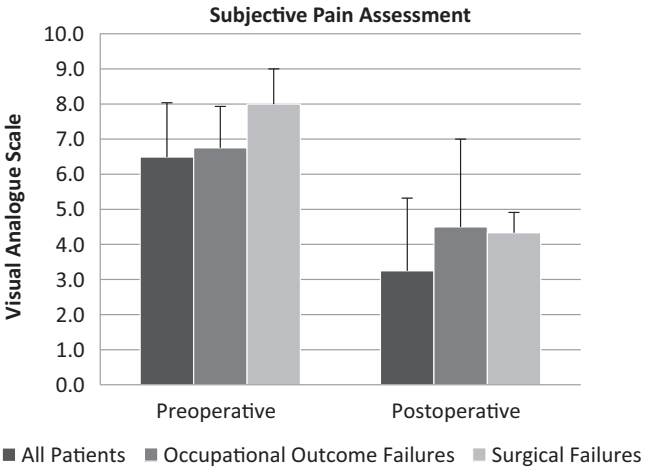

Figure 2. The mean visual analog scale (VAS) pain score demonstrated a significant improvement from 6.5 ± 1.5 (range, 3-10) at baseline to 3.2 ± 2.1 (range, 0-9) postoperatively ($P < .0001$). The occupational outcome failure and surgical failure subgroups had significant improvement in VAS pain scores ($P < .05$). Values are presented as mean ± SD.

TABLE 5
Univariate Logistic Regression Analyses of Occupational Outcome, Surgical, and Overall Failures[a]

	Occupational Outcome Failure		Surgical Failure		Overall Failure	
Univariate Analysis	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age, y[b]	0.87 (0.78-0.97)	**.015**	1.01 (0.83-1.21)	.987	0.86 (0.77-0.97)	**.010**
<30	3.66 (1.10-12.14)	**.034**	1.69 (0.14-19.84)	.677	4.64 (1.41-15.26)	**.011**
Female sex	2.83 (0.69-11.64)	.149	3.39 (0.28-41.30)	.339	4.25 (1.06-17.06)	**.041**
TT-TG distance,[b] mm	0.90 (0.74-1.10)	.309	1.37 (0.78-2.42)	.274	0.90 (0.74-1.10)	.309
≥20	—	—	—	—	—	—
15-19.9	3.27 (0.08-128.52)	.527	1.11 (0.02-52.91)	.960	3.27 (0.08-128.52)	.527
10-14.9	1.70 (0.05-61.15)	.771	0.16 (0.01-13.49)	.414	1.70 (0.05-61.15)	.771
<10	3.71 (0.10-138.85)	.478	0.28 (0.01-25.51)	.580	3.71 (0.10-138.85)	.478
Tobacco use	3.77 (1.15-12.35)	**.028**	0.63 (0.05-7.26)	.710	3.06 (0.99-9.48)	**.050**
BMI,[b] kg/m^2	0.99 (0.85-1.16)	.902	0.86 (0.59-1.24)	.407	0.95 (0.82-1.12)	.557
≥30	1.69 (0.54-5.24)	.367	0.96 (0.08-11.11)	.973	1.48 (0.48-4.52)	.493
Army branch of service	4.90 (0.22-109.95)	.317	0.83 (0.03-21.26)	.909	5.30 (0.24-118.71)	.293
Rank						
Junior enlisted	6.50 (1.01-42.17)	**.049**	0.39 (0.01-11.78)	.586	4.00 (0.73-21.84)	.109
Senior enlisted	1.37 (0.26-7.29)	.713	0.54 (0.06-4.72)	.580	0.84 (0.19-3.69)	.820
Officer/civilian	—	—	—	—	—	—
Military occupational specialty						
Combat arms	0.28 (0.05-1.47)	.132	5.73 (0.21-158.27)	.303	0.28 (0.05-1.47)	.132
Combat support	0.40 (0.11-1.48)	.170	6.70 (0.29-154.02)	.234	0.52 (0.15-1.81)	.307
Combat service support/civilian	—	—	—	—	—	—
Preoperative VAS[b]	1.14 (0.79-1.66)	.475	2.33 (0.84-6.51)	.106	1.24 (0.86-1.80)	.254
Chondral defect location						
Patella	1.31 (0.35-4.86)	.700	0.10 (0.01-2.31)	.151	0.99 (0.29-3.42)	.984
Trochlea	—	—	—	—	—	—
Bipolar	1.69 (0.30-9.36)	.549	1.17 (0.13-10.95)	.890	1.28 (0.24-6.70)	.774
Total defect surface area,[b] cm^2	1.002 (1.000-1.004)	.064	0.999 (0.995-1.004)	.787	1.001 (1.000-1.003)	.119
≥6	13.89 (0.64-302.61)	.094	0.59 (0.05-6.88)	.673	4.26 (0.58-31.25)	.154
4-5.9	3.57 (0.14-91.32)	.441	0.20 (0.01-5.78)	.348	1.10 (0.12-10.21)	.937
2-3.9	12.10 (0.56-261.77)	.112	0.54 (0.05-6.20)	.617	3.71 (0.51-26.93)	.195
<2	—	—	—	—	—	—
Any previous procedures	2.70 (0.78-9.38)	.118	5.58 (0.27-117.44)	.269	3.03 (0.88-10.43)	.079
Previous microfracture procedure	1.96 (0.43-8.91)	.383	3.88 (0.32-47.72)	.290	1.79 (0.40-8.06)	.451
Previous chondroplasty procedure	1.48 (0.49-4.50)	.492	2.83 (0.25-32.67)	.405	1.28 (0.43-3.80)	.662
Concomitant procedure	4.90 (0.22-109.95)	.317	0.83 (0.03-21.26)	.909	5.30 (0.24-118.71)	.293
Concomitant TTO	4.90 (0.22-109.95)	.317	0.83 (0.03-21.26)	.909	5.30 (0.24-118.71)	.293
Periosteal patch	2.38 (0.60-9.47)	.218	51.47 (2.34-1000.00)	**.013**	3.47 (0.91-13.31)	.069

[a]Bold indicates $P < .05$. Dashes indicate the referent variable. BMI, body mass index; OR, odds ratio; TTO, tibial tubercle osteotomy; TT-TG, tibial tubercle–trochlear groove distance; VAS, visual analog scale.
[b]Analyzed as a continuous variable.

second-look arthroscopy. The 4 patients with periosteal graft hypertrophy reported mechanical knee symptoms that required surgical debridement of the graft site, and 3 of these patients eventually met criteria for surgical failure (2 patellofemoral arthroplasty and 1 microfracture). The patient who sustained a displaced proximal tibial fracture at 8 weeks that was attributed to noncompliance with weightbearing and bracing restrictions required open reduction internal fixation.

Univariate logistic regression analysis yielded several risk factors for occupational outcome failure, surgical failure, and overall failure (Table 5). Subsequent multivariate analysis did not isolate any independent risk factors for occupational outcome failure (Table 6). However, use of a periosteal patch was the sole significant predictor of surgical failure (OR, 51.47; 95% CI, 2.34-1000.00) and overall failure (OR, 9.23; 95% CI, 1.19-57.63). Age <30 years (OR, 5.51; 95% CI, 1.33-22.80), regular tobacco use (OR, 7.48; 95% CI, 1.59-35.25), and female sex (OR, 8.91; 95% CI, 1.44-55.01) were significant prognostic factors for overall failure.

DISCUSSION

The current investigation sought to evaluate the outcomes after patellofemoral ACI in a cohort of active patients with moderate to very heavy occupational demands and strenuous physical activity profiles. Symptomatic patellofemoral chondral defects have a detrimental effect on quality of life, work productivity, and overall physical function, particularly among working-age patients. Choosing a procedure that restores hyaline-like cartilage and promotes an

TABLE 6
Multivariate Logistic Regression Analysis for Risk Factors for Surgical and Overall Failures[a]

	Occupational Outcome Failure		Surgical Failure		Overall Failure	
Multivariate Analysis	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age <30 y	—	—	—	—	5.51 (1.33-22.80)	**.019**
Tobacco use	—	—	—	—	7.48 (1.59-35.25)	**.011**
Female sex	—	—	—	—	8.91 (1.44-55.01)	**.019**
Periosteal patch	—	—	51.47 (2.34-1000.00)	**.013**	9.23 (1.19-57.63)	**.033**

[a]Selected multivariate regression analysis performed on variables identified to be $P < .05$ on univariate analysis. Bold indicates $P < .05$. Dashes indicate variables that were not identified as $P < .05$ on univariate analysis. OR, odds ratio.

expeditious return to function is ideal. At a mean follow-up >4 years, 78% of military servicemembers returned to preinjury occupational duties, and the mean reported pain was significantly improved.

Based on objective outcome scores, the success rates in the civilian literature are reported between 73% and 84%[7,25,41,48,49,62] for largely nonpatellar lesions and between 71% and 86% for patellofemoral lesions.[19,21,38] In the only known civilian occupational outcome study after ACI of the knee, Pestka et al[48] reported that 9.2% of patients necessitated workplace adaptations and 10% had to reduce time spent at work to return to preoperative employment. However, this was a comparatively heterogeneous population, with only 23% of patients working in the heavy labor category versus 57% in the current study (heavy/very heavy). Furthermore, the authors failed to analyze outcomes based on chondral defect location (eg, patellofemoral vs tibiofemoral compartments). Within the military, knee-related medical discharge may reflect the inability to reconcile rigorous physical demands with commonly accepted postoperative limitations typically observed for up to 12 months after ACI. US military servicemembers must adhere to mandated semiannual physical fitness testing, including timed runs, and maintain weight and body composition measures.[1,2,36] Servicemembers also have considerable occupational demands, with regularly scheduled aerobic exercises, strength training, and routine essential military tasks, such as marching with 40 lb of equipment, participating in tactical field training, and deploying in austere conditions for up to 12 months.[2] Consequently, this could artificially inflate rates of adverse outcomes, especially occupational outcome failure. Return to gainful employment results in physical and psychosocial health benefits for the individual, as well as a societal economic effect with increased occupational productivity.[5,52]

This study exclusively considered patellofemoral lesions, with most lesions involving the patella (n = 51, 70%). While debated,[12] patellar lesions are suggested to be at an increased risk for surgical failure relative to tibiofemoral articular lesions, in large part because of the unique biomechanical loading environment and variable rates of concomitant distal realignment.[66] Accordingly, the favorable outcomes after ACI for patellofemoral lesions have been much less consistent than those seen in other locations within the knee.[6,21,40,42,49,62,66] Given the inconsistent outcomes after ACI for patellofemoral lesions, further attention has been focused on whether patellar and trochlear chondral defects in isolation have different healing potentials.[16,27,31,38,63] Minas and Bryant[38] prospectively assessed surgical outcomes and collected objective patient-reported outcome scores for patients undergoing first-generation ACI of the knee. At midterm follow-up, the authors reported a significant improvement in the 36-Item Short Form Health Survey Physical Component Summary score, Knee Society Score (knee and function), Western Ontario and McMaster Universities Osteoarthritis Index score, and modified Cincinnati score for isolated patellar chondral defects (n = 8). Isolated trochlear defects (n = 9) had a slightly inferior clinical outcome, with significant improvements only in the modified Cincinnati score. In contrast, isolated patellar lesions had an increased number of surgical failures within the cohort, despite significant improvement in the overall mean of clinical outcome scores. The authors suggested that the increased surgical failure rate of isolated patellar ACI was likely attributable to the high preponderance of patients involved in workers' compensation claims. In a larger separate study of patients undergoing second-generation ACI of the knee,[31] the trochlea (n = 19) and patella (n = 19) groups had 84% and 66% good or excellent results, respectively, on the Cincinnati score at a mean 4-year follow-up. Filardo et al[16] confirmed similar trends in a comparative analysis of patellar and trochlear chondral defects undergoing third-generation ACI. In this study, the patella and trochlea groups had significant improvement in the International Knee Documentation Committee (IKDC), EuroQol VAS, Kujala score, and Tegner score at annual follow-up over 5 years; however, the trochlea subgroup had greater improvement in all categories at each time point. In the current study, we did not identify the presence of an isolated patellar chondral defect as a risk factor for any mode of failure, and there were no significant differences in the rates of overall failures between the isolated patella (9 of 40) and trochlea (5 of 22) cohorts. Furthermore, the isolated patella and isolated trochlea subsets demonstrated a 50% clinical improvement with VAS pain scores ($P < .001$).

Concomitant TTO to correct rotational malalignment or offload selected lesions may synergistically act to improve the outcomes after patellofemoral ACI by normalizing compressive forces and reducing abnormal shear stresses during early remodeling.[3,14,18,19,45,51,62,64] The current study had a large number of knees that underwent concomitant TTO (91%), as is consistent with previous reports concerning patellofemoral ACI.[14,19,21,40] Gillogly and Arnold[19]

reported significant improvements in symptoms and function based on IKDC, modified Cincinnati, Lysholm, and 12-Item Short Form Health Survey scores after ACI for patellar lesions combined with offloading TTO. A subsequent multicenter study similarly evaluated full-thickness focal cartilage lesions of the patellofemoral joint treated with ACI, in which 69% had concomitant TTO. At a minimum 4-year follow-up, 84% of the patients self-rated their knees as improved.[21] In the present series, the overall improvement in patient-reported VAS pain score decreased by 51% from baseline ($P < .0001$) after patellofemoral ACI; more important, similar improvements were also documented among individuals with occupational failure. While these individuals were not able to return to military function, these observed VAS improvements correlate well with clinically significant pain relief.[13,14,50]

Our findings also indicate that patients <30 years of age were more likely to demonstrate an overall failure, similar to a previous report concerning ACI for focal knee chondral defects among military servicemembers.[66] However, other studies reported that younger patients remain preferred candidates for cell-based cartilage knee procedures, owing to the limited adjacent compartment degeneration and improved biological healing capacity.[7,41] A systematic review examining return to sporting activity after surgical treatment of chondral defects among young athletes identified several patient- and defect-specific variables that were predictive of successful functional outcomes.[7] The authors noted that 84% of athletes with focal symptomatic cartilage lesions returned to sport participation after ACI. They concluded that a younger patient age, a smaller chondral defect, a shorter duration of symptoms, native knees, and participation in a dedicated rehabilitation protocol resulted in better outcomes. Additionally, Pestka et al[48] assessed return to sports after ACI and indicated that 73% of patients resumed a sports activity. Further analysis revealed that after ACI, patients most often transitioned from high-impact start-stop sports to more favorable low-impact endurance activities. In the current study's population, these divergent findings may reflect disproportionately greater physical demands associated with younger patient age and junior military status. Furthermore, younger servicemembers often have broader occupational skill sets, lesser degrees of specialized training, and limited mission-critical leadership roles, making them easier to replace. While failure in the general population may be more attributable to age-related decline in cartilage quality and viability, a younger military population is more likely to fail for activity-related reasons and an inability to self-modify occupational activity obligations.

Tobacco use has well-established and detrimental systemic side effects. However, its variable effects on the musculoskeletal system, specifically the articular cartilage, remain ill-defined.[28,32] The current study found that tobacco use was a significant risk factor for overall failure after patellofemoral joint ACI ($P = .005$). A systematic review regarding smoking in shoulder surgery identified the negative influence of nicotine and smoking on rotator cuff repairs.[54] In contrast, previous in vitro studies reported conflicting results regarding the effects of nicotine on chondrocyte health.[23,34] In terms of cartilage restoration, Jaiswal et al[26] reported a clear connection between smoking and negative outcomes with ACI for focal cartilage defects of the knee. The study retrospectively analyzed 3 groups after ACI—cigarette smokers, former smokers, and nonsmokers—with each group followed clinically and undergoing a scheduled second-look arthroscopy at 1 year after surgery. Compared with smokers, nonsmokers experienced significantly greater improvement in the Cincinnati knee score 2 years after surgery and accounted for a significantly higher proportion of good to excellent results on the International Cartilage Repair Society scale during second-look arthroscopy. Furthermore, ACI graft failures were reported only for smokers ($P = .016$), indicating decreased graft incorporation during the early critical maturation period occurring up to 24 months postoperatively.[6,24,26]

The current study revealed an association with patient sex and patellar ACI outcome, with female patients having an increased rate in overall failure after surgery. In a prospective cohort study of 52 patients with ACI of the knee, investigators found that male patients had significantly greater Lysholm scores at all time points and significantly greater IKDC scores at 6 and 12 months.[30] Further subgroup analysis revealed that female patients with patellar lesions had the worst Lysholm and IKDC scores. Filardo et al[17] prospectively followed 250 knees undergoing matrix-assisted ACI with a minimum 5-year follow-up, including a blinded matched-paired analysis of male and female patients (n = 56 each). Within the larger cohort, female patients had significantly lower preoperative Tegner and IKDC scores and a higher percentage of patellar lesions, which may account for the significantly lower final patient-reported outcome scores and cumulative ACI survivorship.

The use of periosteal patch coverage for ACI increased the risk for surgical and overall failure. A clear association of graft hypertrophy and first-generation ACI is well established: an estimated 8% to 50% of patients previously treated with this technique required a secondary debridement.[14,21,22,40,43,66] Further subgroup analysis of the current cohort revealed that 4 of 11 patients undergoing first-generation ACI (36%) required arthroscopic debridement for graft hypertrophy within 18 months after ACI, with 3 of these patients classified as having overall failures. We attribute greater surgical and overall failures with first-generation ACI techniques to a disruption of the hyaline-like cartilage regenerated at the graft site, leading to further abnormalities in the architectural and structural cartilage restoration characteristics.

Previous surgical intervention of articular cartilage defects, specifically marrow stimulation surgery (microfracture, subchondral drilling, or abrasion chondroplasty), before ACI has been clearly identified as a cause for decreased graft survival and clinical outcomes.[27,31,39,40,47,67] In our study, most patients had at least 1 ipsilateral knee surgical procedure before ACI (n = 42, 58%), with 12 having had >1 previous surgical procedure (see Table 3). Prior surgical intervention (see Table 5) failed to achieve statistical significance as a negative prognostic factor for ACI outcomes.

Minas et al[39] compared ACI after previous marrow stimulation techniques among individuals undergoing primary ACI for symptomatic chondral defects and demonstrated an increased failure rate of ACI after marrow stimulation (26%) versus a control group (8%). A prospective multicenter study further demonstrated that despite an increased failure rate for ACI after failed microfracture, patients can still have clinically significant improvements in pain and function.[67] In a retrospective matched-pair study of ACI after failed microfracture versus primary intervention,[47] the prior microfracture group had decreased survival rates (75% vs 96%) and lower scores on the Knee injury and Osteoarthritis Outcome Score subscales for pain and activities of daily living. Similarly, a large single-institution cohort (>400 patients) confirmed a significantly increased risk for failure with >1 previous surgical procedure, and further analysis revealed that any history of a marrow stimulation procedure before ACI almost doubled risk for failure.[27]

Minas et al[40] reported a 62% survival rate of ACI grafts at 15 years among patients with failed marrow stimulation surgery, and patients with prior microfracture (44%) had significantly worse survivorship than those with primary ACI (79%). Many theorize that the normal subchondral plate architecture is disrupted at the time of previous marrow stimulation, which can lead to subsequent reactive osseous overgrowth within the cartilage defect, effectively creating pathology in the osteochondral unit. In the current series, chondroplasty was preferentially performed at the time of the index procedure (60%) and microfracture was less commonly performed, given its limited success in the patellofemoral joint; these factors may account for the relative disparity in reported risk factors for patellofemoral ACI failure.

The strengths of this study include the closed health care system, universally mandated physical fitness requirements, and intense occupational demands for active duty servicemembers undergoing patellofemoral ACI. However, certain limitations must also be recognized. First, the definition of clinical failure may be overly stringent and lack external validity to less active or sedentary patient populations. Second, there is the potential for nonresponder bias with patients who complete their military service obligation and exit the military or choose to follow up in the civilian health care network. Third, the current study lacks validated patient-reported outcomes other than the VAS, which would increase the generalizability of our findings and allow for quantification of functional outcomes. Last, there was a high rate of concomitant TTO, which could introduce selection bias and confounding in reporting high rates of return to previous level of activity. Because most patients also had a TTO procedure, it is not possible to determine how much improvement was caused by the ACI and how much by the TTO.

CONCLUSION

Patellofemoral ACI offers young, highly active patients an appealing reproducible option for isolated patellofemoral chondral defects. Approximately 78% of military patients returned to preinjury occupational function and had a low revision rate (4.1%). Significant risk factors for overall failure after patellofemoral ACI were age <30 years, female sex, and tobacco use, while first-generation periosteal ACI patch use was associated with surgical and overall failures.

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