

Utilization of Autologous Chondrocyte Implantation in the Knee is Increasing While Reoperation Rates Are Decreasing Despite Increasing Preoperative Comorbidities

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Purpose: The primary purpose of this study was to assess the use of autologous chondrocyte implantation (ACI) procedures in the knee during last decade, and the secondary aims of the study were to determine reoperation rates after ACI and to identify associated risk factors. **Methods:** A retrospective cohort study from 2010–2020 was performed using the PearlDiver database. The database was queried for the Current Procedural Terminology (CPT) code for ACI performed in any knee location, including the patellofemoral and tibiofemoral joints. Reoperation was defined as interventional knee procedures or total knee arthroplasty after ACI. Reoperations were identified using CPT and International Classification of Diseases codes. Univariate and multivariate logistic regression were used to identify risk factors for reoperation. Significance was defined as $P < .05$. **Results:** Among the 2010 patients included in this study, there were 90-day and overall reoperation rates of 2.24% and 30.4%, respectively, with an average follow up of 4.8 ± 3.3 years. The most common reoperations included chondroplasty, meniscectomy, and microfracture. There was an increased rate of ACI performed from 2017–2019 (5.53/100,000) compared to 2014–2016 (4.16/100,000; $P < .001$). ACI surgeries performed in 2017–2019 were associated with decreased risk of reoperation within 2 years relative to 2014–2016 (odds ratio [OR] = 0.70; 95% confidence interval [CI], 0.52-0.94; $P = .019$). In the entire ACI cohort, older age (OR = 1.07; 95% CI, 1.05-1.09; $P < .001$) and tobacco use (OR = 2.13; 95% CI, 1.06-3.94; $P = .022$) were associated with increased risk of conversion to arthroplasty. Male sex was associated with decreased overall reoperation rates (OR = 0.73; 95% CI, 0.60-0.89; $P = .002$). **Conclusions:** There has been increasing use of ACI in the knee with decreased risk of reoperation since 2017 and the introduction of matrix-associated autologous chondrocyte implantation. Older age and tobacco use were predictors of increased risk of conversion to arthroplasty. Male sex was associated with decreased risk of reoperation. **Level of Evidence:** Level IV, retrospective cohort design; database study.

Articular cartilage and osteochondral injuries of the knee joint are common and can result in significant pain and knee dysfunction.¹⁻³ Previous studies have reported chondral lesions in up to 65% of knees at the time of diagnostic arthroscopy.⁴⁻⁶ Over the last few

decades, the treatment of articular cartilage defects has evolved as restorative cartilage procedures, such as autologous chondrocyte implantation (ACI) and osteochondral auto/allograft transplantations, have been developed. The annual incidence of articular

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cartilage surgeries among all orthopaedic surgeries performed in the United States has been estimated at 5%, with a recent increase in these restorative procedures relative to procedures such as chondroplasty or microfracture.^{7,8}

Among restorative cartilage procedures, a systematic review demonstrated that third-generation or matrix-associated autologous chondrocyte implantation (MACI) has become favored in recent years in the setting of full-thickness articular cartilage defects of the knee.⁹ The current generation of MACI was introduced relatively recently in the United States, with Food and Drug Administration approval received in December 2016. This newly approved implant offers autologous chondrocytes cultured on a porcine collagen membrane and can be implanted with a generally simpler process than prior generations of ACI that required suturing a collagen patch.¹⁰

The understanding of complications and reoperation with regards to ACI/MACI is overall limited. In national database studies evaluating trends in articular cartilage surgeries in the United States, data from patients with ACI and osteochondral auto/allograft transplantations are usually combined, thus limiting our ability to directly interpret ACI utilization rates.^{7,8} Additionally, few studies have investigated reoperation rates after ACI and the risk factors associated with this specific technique in a large cohort of patients. Most existing data are from single-institutions or review articles which examine studies with different definitions of failure or significant reoperation.¹¹⁻¹⁵ Generalizable data on the prevalence and predictors of reoperations after ACI in the United States are lacking.

The primary purpose of this study was to assess the use of ACI procedures in the knee during last decade, and the secondary aims of the study were to determine reoperation rates after ACI and to identify associated risk factors. We hypothesized that there will be significantly higher rates of ACI procedures performed after 2017 among the general population due to the recent introduction of MACI. Additionally, given the relative ease of MACI compared to its predecessors, we also hypothesized that there would be increased reoperation rates among the total amount of patients who had ACI performed after 2017 because of the selection of more complicated patients for cartilage restoration surgery.

Methods

The PearlDiver Mariner Database (PearlDiver Technologies Inc, Colorado Springs, CO) was used to conduct this retrospective study. It contains insurance claims records from 91 million patients in the United States between 2010 and 2020 and encompasses a diverse set of payer types, such as Medicaid, Medicare, commercial entities, government, and cash payment. This dataset was queried using codes from the

International Classification of Diseases (ICD), 9th Revision (ICD-9), 10th Revision (ICD-10), and Current Procedural Terminology (CPT). This study did not require ethics committee approval according to the national law.

Identification of Autologous Chondrocyte Implantation Procedures

Data were queried from the MArthro dataset, which is a subset of approximately 4 million patients within the Mariner dataset. To be included in the study, patients needed a CPT code for ACI (CPT-27412) in their record. The CPT includes ACI procedures for lesions in all compartments of the knee, including the patellofemoral and tibiofemoral joints.

Identification of Reoperations: Interventional Knee Procedures and Total Knee Arthroplasty

Patient records were queried for subsequent interventional knee procedures and total knee arthroplasty (TKA) (Appendix Table 1). Interventional knee procedures were defined as: interventional knee arthroscopy, osteochondral autograft, osteochondral allograft, lavage and drainage for infection, foreign body removal, synovectomy, chondroplasty, meniscal transplantation, meniscectomy, meniscus repair, lysis of adhesions, drilling for osteochondritis dissecans, anterior cruciate ligament reconstruction, microfracture, high tibial osteotomy, distal femoral osteotomy, arthrotomy in the knee, collateral and cruciate ligament repairs/reconstructions, extra-/intra-articular ligament reconstructions, and open reconstruction surgery for knee dislocation. CPT code 29870 was used to identify patients who had an isolated diagnostic knee arthroscopic procedure after ACI. Diagnostic knee arthroscopic procedures were excluded from the analysis of interventional knee reoperation procedures.

Patients were tracked for 90 days and to the date of last follow-up after ACI, and those with codes for TKA or interventional knee procedures were included in the "reoperation" group (experimental group), whereas patients with no such codes were included in the "no reoperation" group (control group).

Baseline characteristics were collected for the experimental and control groups. The database was queried for demographic factors to compare the groups, which included age, Charlson Comorbidity Index (CCI), sex, tobacco use, diabetes, and body mass index (BMI) (Appendix Table 2). The CCI is a widely used and validated adjustment index that accounts for multiple comorbidities to provide an overall assessment of a patient's health.¹⁶ A patient was classified as having a medical comorbidity (obesity, tobacco use, or diabetes) if they had a CPT or ICD diagnostic code for the comorbidity in their record within the 1 year before or on the same day as the ACI.

Comparing Utilization and Reoperation Rates before and after 2017

To evaluate MACI utilization and reoperation rates after its introduction in 2017 as compared to ACI use and reoperation before 2017, patient records in 2014–2016 and 2017–2019 were queried for the first instance of the CPT code for ACI in the database and were split into their two respective groups. The period of 2014–2016 compared to 2017–2019 was selected to standardize ACI follow-up times before and after 2017 and reduce the potential for the length of follow-up to be a confounder. Population data were gathered from

PearlDiver to calculate the annual rates of ACI procedures performed. Patients were tracked for reoperations within 90 days and 2 years after ACI.

Baseline characteristics were collected for the groups of patients who had ACI performed in 2014–2016 and 2017–2019. The database was queried for patient demographic factors to compare the 2 groups, including age, CCI, sex, tobacco use, diabetes, and BMI.

Statistical Analysis

Statistical analysis was performed using the PearlDiver software, which uses R software for the analysis.

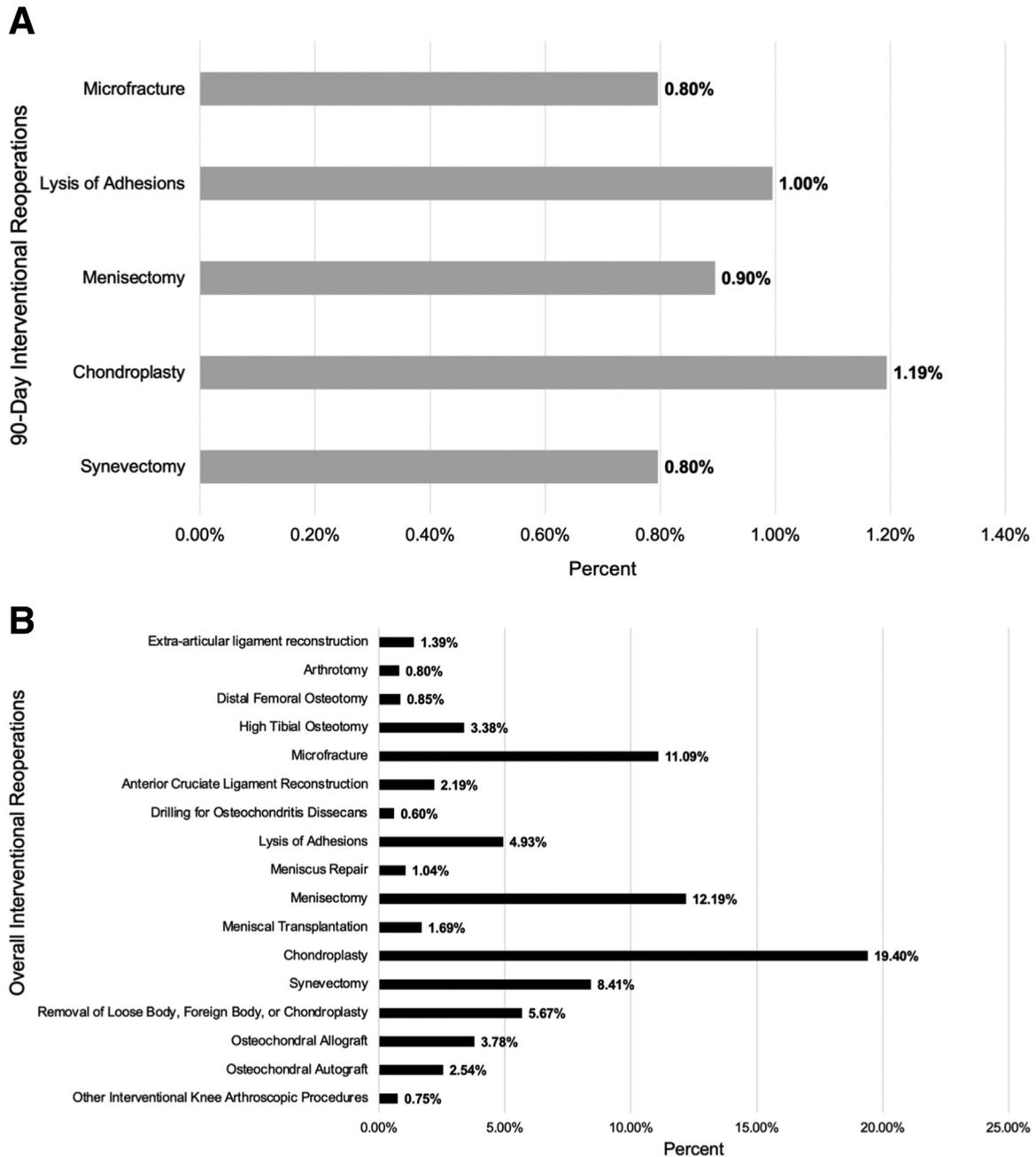


Fig 1. Rates of 90-day (A) and overall (B) interventional reoperations performed after ACI among the total population of patients who have undergone ACI.

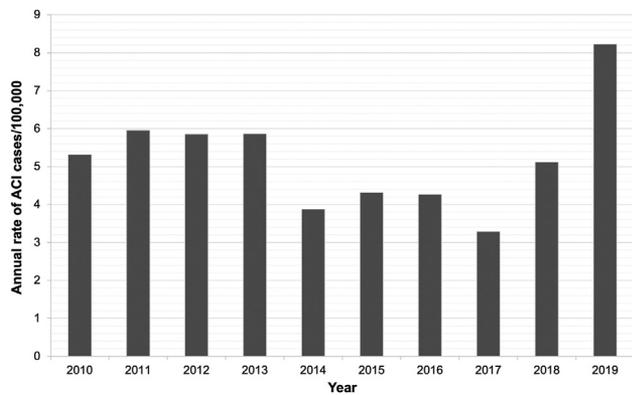


Fig 2. The annual rate of ACI procedures performed among the total amount of patients in the PearlDiver MArthro Dataset from 2010–2019.

All analyses were considered significant with a P value $< .05$. Welch's t -test was used to compare continuous variables between groups. The χ^2 tests were used to compare categorical variables. Univariate logistic regression was used to calculate associations between possible risk factors and reoperations. Age, CCI, male sex, tobacco use, diabetes, and obesity were the variables run for reoperations that were evaluated in univariate regression. ACI performed between 2017–2019 was an additional variable analyzed with regards to two-year reoperations in univariate regression. Odds ratios (OR) and 95% confidence intervals (CI) were calculated from the univariate logistic regression analysis. Univariate logistic regression was not performed when there were fewer than 11 patients for a given reoperation because of limitations of the database.

Multivariate logistic regression was then performed, including only variables with a P value $< .05$ from the univariate regression. Adjusted ORs and CIs were calculated from the multivariate logistic regression.

Results

Demographics of ACI and Subsequent Reoperations

Among the entire MArthro population, 2010 patients who underwent ACI between 2010 and 2020 were

included in this study. There was an average follow up time of 4.8 ± 3.3 years. The most common reoperations performed on patients within 90 days after ACI were chondroplasty (1.19%, $N = 24$), lysis of adhesions (1.00%, $N = 20$), and meniscectomy (0.90%, $N = 18$) (Fig 1A). By last follow-up, the most common reoperations performed were chondroplasty (19.4%, $N = 390$), meniscectomy (12.2%, $N = 245$), and microfracture (11.1%, $N = 223$) (Fig 1B).

Table 1 summarizes the demographic characteristics of the reoperation group and those who underwent ACI without subsequent reoperation. The 90-day reoperation rate after ACI was 2.24%. For reoperations within 90 days after ACI, patients were only more likely to be female ($P = .028$). The overall reoperation rate after ACI was 30.4%. Patients in the reoperation group were more likely to be older and female (Table 1). The interventional knee procedure reoperation rate was 2.14% ($N = 43$) and 28.8% ($N = 579$) within 90 days and the overall time-period after ACI, respectively. The TKA reoperation rate was 0.1% ($N = 2$) and 4.48% ($N = 90$) within 90 days and the overall time period after ACI, respectively. The diagnostic knee arthroscopic reoperation rate was 1.49% ($N = 30$) in the overall time after ACI.

ACI Utilization Rates

The annual rates of ACI procedures performed relative to the entire population is plotted in Fig 2. There was a significant increase in the rate of ACIs performed within the total population of patients in the MArthro dataset of PearlDiver from 2017–2019 (5.53/100,000) relative to 2014–2016 (4.16/100,000; $P < .0001$).

Patients in the 2017-2019 ACI cohort were more likely to have a higher CCI and be obese than those in the 2014-2016 cohort; however, they were less likely to have a history of tobacco use (Table 2). The 90-day reoperation rate was 3.80% (17/447) and 0.68% (4/584) in the 2014–2016 and 2017–2019 ACI cohorts, respectively. The 90-day reoperation rate from 2017–2019 was significantly lower compared to the reoperation rate for 2014–2016 ($P = .0004$). The 2-year reoperation rate was similarly significantly lower in 2017–2019 (20.2%) relative to 2014–2016 (26.2%; $P = .024$).

Table 1. Demographic Data of ACI Patients with 90-Day and Overall Reoperations

	Within 90 Days			Overall		
	No Reoperation (N = 1965)	Reoperation (N = 45)	P	No Reoperation (N = 1398)	Reoperation (N = 612)	P
Age	34.1 \pm 11.8	36.6 \pm 11.6	.154	33.8 \pm 12.1	35.0 \pm 11.1	.037
CCI	0.45 \pm 0.95	0.84 \pm 1.57	.101	0.46 \pm 0.95	0.47 \pm 1.00	.830
Male Sex	870 (44.3%)	12 (26.7%)	.028	647 (46.3%)	235 (38.4%)	.001
Tobacco Use	132 (6.72%)	<11	.370	84 (6.01%)	49 (8.01%)	.119
Diabetes	89 (4.53%)	<11	.707	67 (4.79%)	23 (3.76%)	.360
Obesity	205 (10.4%)	<11	.930	142 (10.2%)	67 (10.9%)	.649

All values represent mean \pm standard deviation or n (percentage).

Table 2. Demographic Data of Patients Who Had ACI Performed in 2014 to 2016 and 2017 to 2019

	ACI Performed in 2014–2016 (N = 447)	ACI Performed in 2017–2019 (N = 584)	P
Age	34.1 ± 11.5	32.9 ± 11.2	.085
CCI	0.38 ± 0.82	0.57 ± 0.93	<.001
Male Sex	199 (44.5%)	240 (41.1%)	.299
Tobacco Use	37 (8.28%)	15 (2.57%)	<.001
Diabetes	19 (4.25%)	23 (3.94%)	.926
Obesity	33 (7.38%)	75 (12.8%)	.006

All values represent mean ± standard deviation or n (percentage).

Table 3 includes the odds of 2-year reoperations among patients who had ACI performed between 2014 to 2019. On univariate analysis, male sex and having an ACI performed between 2017–2019 were both associated with lower odds of 2-year reoperations. These findings remained significant in the multivariate analysis (Table 3).

ORs of ACI Reoperations (TKA and Interventional Procedures) in the Entire Population

Table 4 summarizes the odds of both overall and TKA reoperations after ACI by the time of last follow-up. Older age was associated with higher odds of overall reoperations whereas male sex was associated with lower odds of reoperation in the univariate analysis. After adjusting for possible confounders, male sex was independently associated with lower odds of overall reoperation after ACI (Table 4). For the odds of conversion to knee arthroplasty in the overall time after ACI, older age and tobacco use were associated with higher odds of conversion to arthroplasty, whereas male sex was associated with lower odds of reoperation on univariate analysis. Multivariate analysis yielded the same results (Table 4). For the odds of reoperations for interventional knee procedures in the overall time after ACI, male sex was independently associated with lower odds of reoperation in the univariate analysis (OR = 0.71; 95% CI, 0.58-0.87; $P < .001$).

Discussion

In this large cohort of patients, we observed a significant increase in the use of ACI since 2017. There was a significant decrease in the rate of 90-day and 2-year reoperations for ACIs performed after 2017 despite the observed increase in use during this time. Patients selected for ACI after 2017 were more likely to be obese and have medical comorbidities but, however, less likely to be tobacco smokers. ACIs performed in 2017–2019 were associated with decreased risk of a reoperation within 2 years relative to those performed in 2014–2016. In the entire population of patients who had ACI performed, there was a 90-day reoperation rate of 2.24% and an overall reoperation rate of 30.4%

with an average follow-up of 4.8 years. Older age and tobacco use were associated with higher rates of conversion to arthroplasty in the overall time after ACI. Male sex was predictive of decreased likelihood of reoperation for all procedures by the time of last follow-up.

In alignment with our hypothesis and also to what had been suggested in a recent systematic review, which included 708 patients,⁹ our study found a significant upwards trend in the annual rate of ACI procedures performed after 2017 as compared to prior years. There was an increase of operative rates by nearly 60% from 2018 to 2019. These findings are likely the result of the introduction of recent implant technology which came about with the Food and Drug Administration approval of MACI in December 2016. Compared to prior generations of ACI, MACI has a shorter and more simplified implantation process because of the direct application of chondrocytes to the membrane and the ability to secure the membrane with fibrin glue rather than sutures.¹⁷ Thus the procedure is often technically easier to perform and may be adopted more broadly by surgeons. As such, this study found that patients with obesity and other medical comorbidities were more likely to be selected as candidates for ACI after the introduction of the current generation of MACI. However, despite the increased selection of more complex patients in recent years, this study observed (1) reduced 90-day and 2-year reoperation rates, and (2) an association with decreased risk of reoperation within 2 years in the cohort of patients who underwent operation after 2017. These findings suggest that early results with MACI may yield more favorable postoperative outcomes than first- or second-generation ACI.

Reoperation rates after ACI vary widely in the literature. Recent studies have reported reoperation rates to be between 5% and 67.6%, although follow-up time and the specific reoperations included in overall reoperation rates vary.^{13–15,18,19} Our finding of an overall reoperation rate of 30.4% is similar to the results

Table 3. Odds of 2-Year Reoperations (Interventional Procedures and Total Knee Arthroplasty) Between 2014 to 2019

	Univariate Analysis		Multivariate Analysis	
	OR [95% CI]	P	AOR [95% CI]	P
ACI Performed in 2017-2019	0.72 [0.54-0.97]	.028	0.70 [0.52-0.94]	.019
Age	1.01 [1.00-1.02]	.306	—	—
CCI	1.10 [0.94-1.28]	.235	—	—
Male sex	0.52 [0.38-0.71]	<.001	0.52 [0.38-0.70]	<.001
Tobacco use	1.26 [0.65-2.31]	.478	—	—
Diabetes	0.55 [0.21-1.23]	.181	—	—
Obesity	1.14 [0.71-1.79]	.581	—	—

AOR, adjusted odds ratio.

Table 4. Odds of Reoperation by the Time of Last Follow-up: Overall Reoperations and Total Knee Arthroplasty Only

	Overall Reoperations				Total Knee Arthroplasty			
	Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
	OR [95% CI]	<i>P</i>	AOR [95% CI]	<i>P</i>	OR [95% CI]	<i>P</i>	AOR [95% CI]	<i>P</i>
Age	1.01 [1.00-1.02]	.044	1.01 [1.00-1.02]	.067	1.07 [1.05-1.09]	<.001	1.07 [1.05-1.09]	<.001
CCI	1.01 [0.91-1.11]	.827	—	—	1.08 [0.87-1.28]	.463	—	—
Male sex	0.72 [0.60-0.88]	.001	0.73 [0.60-0.89]	.002	0.53 [0.33-0.84]	.007	0.56 [0.35-0.89]	.017
Tobacco use	1.36 [0.94-1.95]	.098	—	—	2.29 [1.16-4.16]	.011	2.13 [1.06-3.94]	.022
Diabetes	0.78 [0.47-1.24]	.303	—	—	1.27 [0.44-2.92]	.614	—	—
Obesity	1.09 [0.80-1.47]	.593	—	—	1.35 [0.69-2.42]	.352	—	—

AOR, adjusted odds ratio.

reported in a systematic review of multiple medical databases that found a 33% overall reoperation rate among 5276 subjects.¹⁴ Our study also examined the prevalence of 90-day reoperation rates among the ACI population. In this cohort, patients had a 2.24% 90-day reoperation rate, with the most common reoperation procedure being chondroplasty, both in the 90-day timeframe and at final follow-up.

This study identified an association between male sex and decreased reoperation rates. The influence sex has on the outcomes of cartilage restoration surgeries has been well described in other studies.²⁰⁻²⁵ A prospective study out of a single center observed that isokinetic muscle strength measures of the treated knee were significantly worse in women at 48 months after autologous chondrocyte implantation.²² The difference in chondral volume between sexes has been cited as one potential causes for the poorer outcomes seen in females after ACI and other cartilage surgeries done in the knee.²¹ The influence of patient sex on the differences in knee cartilage volume tend to be more pronounced with increased age, specifically above 40.²⁶ As such, surgeons may counsel male and female patients differentially with regard to the potential need for subsequent surgery after ACI.

Tobacco use was found to be a risk factor with greater than 2-fold increased odds for conversion to arthroplasty following ACI. Regarding tobacco use among ACI patients, the relationship with reoperations after the surgery are unclear because there are contradicting conclusions reported in the current literature. Jaiswal et al.²⁷ reported that there was an association between smoking and worse patient-reported outcomes (PROs) and that it was predictive of graft failure after ACI in a retrospective study of 129 adults.²⁷ Similarly, Zarkadis et al.²⁸ also found an increased rate of graft failure among smoking ACI patients in another small study of 72 patients. However, in a recent 2020 national database study similar to our own, Sochacki et al.¹⁹ found no association between tobacco use and overall reoperation rates. Their study included 315 patients with autologous chondrocyte implantation compared to our

2010. Additionally, the findings of their study do not contradict our own. Contrary to our methods, they do not break down the reoperations in their analysis, so the lack of an association was noted for the total reoperations. For total reoperations in this study, we made the same observation and only found tobacco use to be predictive of conversion to TKA in the overall time after ACI, which represented less than 5% of total reoperations. Our larger cohort and analysis methods provide stronger evidence for tobacco use as a risk factor for reoperation and can be used to help educate patients on the benefit of smoking cessation for better outcomes after ACI. Because of its association with an increased risk of conversion to arthroplasty, it is recommended that patients quit smoking before surgery.

In addition to tobacco use, we found that age was also a key predictor for increased risk of subsequent conversion to arthroplasty among the ACI cohort. Each increase in year was associated with a 7% increase in odds of TKA. Prior studies have similarly noted the association of increased age and increased risk of reoperation, failure, and worse PROs after ACI.^{12,13} Generally, arthroplasty becomes a more viable treatment option in older patients, whereas younger patients are more likely to undergo other procedures such as high tibial osteotomy to preserve the joint.^{29,30} However, the quality of chondrocytes at biopsy is another possible implication to consider. Barbero et al.³¹ found a 1.8-fold decrease in chondrocyte yield in donors older than 40 years of age. The findings from these preliminary studies and our study imply that ACI has better postoperative outcomes in younger patients. This can help guide surgeons in choosing an effective treatment option that is best tailored to their patient's individual needs.

In this study, obesity was not found to be a significant predictor of increased risk of reoperations in this population. It is worth noting that only 10% of the patients in our cohort were obese. For ACI, obesity has been designated as a contraindication to operation, with the recommendation for patients to be within at least 10% of their ideal BMI at surgery and afterward to avoid

complications. In a prospective study of 122 patients, Jaiswal et al.³² found that obese patients demonstrated no sustained improvement in PROs 2 years after ACI/MACI, whereas patients with an ideal body weight experienced significant improvement as early as 6 months after. Additionally, a negative correlation between BMI and MRI-based outcomes, such as graft infill and joint effusion, was found in a randomized controlled study of 70 patients.³³ Contrary to those findings, Ebert et al.³⁴ found no correlation between BMI and patient outcomes in a retrospective study of 104 patients. However, only 20% of the patients investigated in that study were obese because those with a BMI greater than 35 were excluded. Therefore the lack of an association between obesity and reoperations in this study was likely a result of selection bias in this cohort because of effective preoperative risk stratification by surgeons.

Limitations

An important limitation of this study is related to its retrospective nature and analysis of patients in a large national database. Like all large database studies, miscoding and noncoding in the documentation completed by providers are potential sources of error in our results. Additionally, we were unable to evaluate the potential association between preoperative and postoperative PROs and reoperations after ACI in this retrospective analysis of records. The current CPT code that is routinely used for ACI presented additional limitations. Given that only one code is available, we were unable to breakdown and analyze individual autologous chondrocyte implantation techniques, such as first-, second-, and third-generation ACI. These technical differences may influence outcomes in ways that could not be discerned in this study. Furthermore, many of the patients were identified using CPT and ICD-9 codes, which do not specify laterality. Therefore we were unable to track which side the ACI and reoperations occurred on, and it was not possible to be certain that the subsequent surgery was performed on the same side as the ACI.

Conclusions

There has been increasing use of ACI in the knee with decreased risk of reoperation since 2017 and the introduction of MACI. Older age and tobacco use were predictors of increased risk of conversion to arthroplasty. Male sex was associated with decreased risk of reoperation.

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References

1. Buckwalter JA. Articular cartilage: Injuries and potential for healing. *J Orthop Sports Phys Ther* 1998;28:192-202.
2. Bhosale AM, Richardson JB. Articular cartilage: Structure, injuries and review of management. *Br Med Bull* 2008;87:77-95.
3. Takeda H, Nakagawa T, Nakamura K, Engebretsen L. Prevention and management of knee osteoarthritis and knee cartilage injury in sports. *Br J Sports Med* 2011;45:304-309.
4. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: A review of 31,516 knee arthroscopies. *Arthroscopy* 1997;13:456-460.
5. Årøen A, Løken S, Heir S, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. *Am J Sports Med* 2004;32:211-215.
6. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. *Arthroscopy* 2002;18:730-734.
7. McCormick F, Harris JD, Abrams GD, et al. Trends in the surgical treatment of articular cartilage lesions in the United States: An analysis of a large private-payer database over a period of 8 years. *Arthroscopy* 2014;30:222-226.
8. DeFroda SF, Bokshan SL, Yang DS, Daniels AH, Owens BD. Trends in the surgical treatment of articular cartilage lesions in the United States from 2007 to 2016. *J Knee Surg* 2021;34:1609-1616.
9. Shanmugaraj A, Coughlin RP, Kuper GN, et al. Changing trends in the use of cartilage restoration techniques for the patellofemoral joint: A systematic review. *Knee Surg Sports Traumatol Arthrosc* 2019;27:854-867.
10. Barić A, Kruck P, Sorbi R, et al. Prospective long-term follow-up of autologous chondrocyte implantation with periosteum versus matrix-associated autologous chondrocyte implantation: A randomized clinical trial. *Am J Sports Med* 2020;48:2230-2241.
11. Everhart JS, Jiang EX, Poland SG, Du A, Flanigan DC. Failures, reoperations, and improvement in knee symptoms following matrix-assisted autologous chondrocyte transplantation: A meta-analysis of prospective comparative trials. *Cartilage* 2021;13(1_suppl):1022S-1035S.
12. McNickle AG, L'Heureux DR, Yanke AB, Cole BJ. Outcomes of autologous chondrocyte implantation in a diverse patient population. *Am J Sports Med* 2009;37:1344-1350.
13. Pareek A, Carey JL, Reardon PJ, Peterson L, Stuart MJ, Krych AJ. Long-term outcomes after autologous chondrocyte implantation: A systematic review at mean follow-up of 11.4 years. *Cartilage* 2016;7:298-308.
14. Harris JD, Siston RA, Brophy RH, Lattermann C, Carey JL, Flanigan DC. Failures, re-operations, and complications after autologous chondrocyte implantation—A systematic review. *Osteoarthritis Cartilage* 2011;19:779-791.
15. Wylie JD, Hartley MK, Kapron AL, Aoki SK, Maak TG. Failures and reoperations after matrix-assisted cartilage repair of the knee: A systematic review. *Arthroscopy* 2016;32:386-392.
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in

- longitudinal studies: Development and validation. *J Chronic Dis* 1987;40:373-383.
17. Zeifang F, Oberle D, Nierhoff C, Richter W, Moradi B, Schmitt H. Autologous chondrocyte implantation using the original periosteum-cover technique versus matrix-associated autologous chondrocyte implantation: A randomized clinical trial. *Am J Sports Med* 2010;38:924-933.
 18. Niemeyer P, Schubert T, Grebe M, Hoburg A. Matrix-associated chondrocyte implantation is associated with fewer reoperations than microfracture: Results of a population-representative, matched-pair claims data analysis for cartilage defects of the knee. *Orthop J Sports Med* 2019;7(10):2325967119877847.
 19. Sochacki KR, Varshneya K, Calcei JG, et al. Comparison of autologous chondrocyte implantation and osteochondral allograft transplantation of the knee in a large insurance database: Reoperation rate, complications, and cost analysis. *Cartilage* 2021;13(1_suppl):1187S-1194S.
 20. Andriolo L, Reale D, Di Martino A, et al. Long-term results of arthroscopic matrix-assisted autologous chondrocyte transplantation: A prospective follow-up at 15 years. *Am J Sports Med* 2020;48:2994-3001.
 21. Filardo G, Kon E, Andriolo L, et al. Does patient sex influence cartilage surgery outcome? Analysis of results at 5-year follow-up in a large cohort of patients treated with matrix-assisted autologous chondrocyte transplantation. *Am J Sports Med* 2013;41:1827-1834.
 22. Kreuz PC, Müller S, Erggelet C, et al. Is gender influencing the biomechanical results after autologous chondrocyte implantation? *Knee Surg Sports Traumatol Arthrosc* 2014;22:72-79.
 23. Kreuz PC, Müller S, von Keudell A, et al. Influence of sex on the outcome of autologous chondrocyte implantation in chondral defects of the knee. *Am J Sports Med* 2013;41:1541-1548.
 24. Krishnan SP, Skinner JA, Bartlett W, et al. Who is the ideal candidate for autologous chondrocyte implantation? *J Bone Joint Surg Br* 2006;88-B:61-64.
 25. Jungmann PM, Salzmann GM, Schmal H, et al. Autologous chondrocyte implantation for treatment of cartilage defects of the knee: What predicts the need for reintervention? *Am J Sports Med* 2012;40:58-67.
 26. Ding C, Cicuttini F, Blizzard L, Scott F, Jones G. A longitudinal study of the effect of sex and age on rate of change in knee cartilage volume in adults. *Rheumatology* 2007;46:273-279.
 27. Jaiswal PK, Macmull S, Bentley G, et al. Does smoking influence outcome after autologous chondrocyte implantation? a case-controlled study. *J Bone Joint Surg Br* 2009;91:1575-1578.
 28. Zarkadis NJ, Belmont PJ, Zachilli MA, et al. Autologous chondrocyte implantation and tibial tubercle osteotomy for patellofemoral chondral defects: Improved pain relief and occupational outcomes among US Army service-members. *Am J Sports Med* 2018;46:3198-3208.
 29. Brinkman JM, Lobenhoffer P, Agneskirchner JD, et al. Osteotomies around the knee. *J Bone Joint Surg Br* 2008;90-B:1548-1557.
 30. Kucirek NK, Anigwe C, Zhang AL, Ma CB, Feeley BT, Lansdown DA. Complications after high tibial osteotomy and distal femoral osteotomy are associated with increasing medical comorbidities and tobacco use [published online February 3, 2022]. *Knee Surg Sports Traumatol Arthrosc*. <https://doi.org/10.1007/s00167-022-06865-z>.
 31. Barbero A, Grogan S, Schäfer D, Heberer M, Mainil-Varlet P, Martin I. Age related changes in human articular chondrocyte yield, proliferation and post-expansion chondrogenic capacity. *Osteoarthritis Cartilage* 2004;12:476-484.
 32. Jaiswal PK, Bentley G, Carrington RWJ, Skinner JA, Briggs TWR. The adverse effect of elevated body mass index on outcome after autologous chondrocyte implantation. *J Bone Joint Surg Br* 2012;94-B:1377-1381.
 33. Ebert JR, Fallon M, Robertson WB, et al. Radiological assessment of accelerated versus traditional approaches to postoperative rehabilitation following matrix-induced autologous chondrocyte implantation. *Cartilage* 2011;2:60-72.
 34. Ebert JR, Smith A, Edwards PK, Hambly K, Wood DJ, Ackland TR. Factors predictive of outcome 5 years after matrix-induced autologous chondrocyte implantation in the tibiofemoral joint. *Am J Sports Med* 2013;41:1245-1254.

Appendix Table 1. Codes Used to Define Total Knee Arthroplasty, Diagnostic Knee Arthroscopy, and Interventional Knee Procedures

Procedure	Code
Total knee arthroplasty	CPT-27447, CPT-27486, CPT-27487, ICD-9-P-8154, ICD-10-P-0SRD0J9, ICD-10-P-0SRC0J9, ICD-10-P-0SRC0JA, ICD-10-P-0SRD0JA, ICD-10-P-0SRC069, ICD-10-P-0SRC06A, ICD-10-P-0SRC06Z, ICD-10-P-0SRC0JZ, ICD-10-P-0SRD069, ICD-10-P-0SRD06A, ICD-10-P-0SRD06Z, ICD-10-P-0SRD0JZ
Diagnostic knee arthroscopy	CPT-29870
Interventional knee procedures	
Interventional knee arthroscopy	ICD-9-P-8026, ICD-10-P-0SJC4ZZ, ICD-10-P-0SJD4ZZ
Osteochondral autograft	CPT-29866, CPT-29867, CPT-27416
Osteochondral allograft	CPT-27415
Infection, lavage, and drainage	CPT-29871
Foreign body removal	CPT-29874, CPT-G0289
Synovectomy	CPT-29875, CPT-29876, ICD-9-8076
Chondroplasty	CPT-29877
Meniscal transplantation	CPT-29868
Meniscectomy	CPT-29880, CPT-29881, ICD-9-P-806
Meniscus repair	CPT-29882, CPT-29883
Lysis of adhesions	CPT-29884
Drilling for osteochondritis dissecans	CPT-29885, CPT-29886, CPT-29887
Anterior cruciate ligament repair	CPT-29888
Microfracture	CPT-29873, CPT-29879
High tibial osteotomy	CPT-27457, CPT-27455, CPT-27705, CPT-27709, ICD-9-P-7727, ICD-10-P-0Q8G0ZZ, ICD-10-P-0Q8G3ZZ, ICD-10-P-0Q8G4ZZ, ICD-10-P-0Q8H0ZZ, ICD-10-P-0Q8H3ZZ, ICD-10-P-0Q8H4Z
Distal femoral osteotomy	CPT-27140, CPT-27448, CPT-27450, ICD-9-P-7725, ICD-10-P-0Q8B0ZZ, ICD-10-P-0Q8C0ZZ, ICD-10-P-0Q8C3ZZ, ICD-10-P-0Q8C4ZZ, ICD-10-P-0Q8B3ZZ, ICD-10-P-0Q8B4ZZ
Arthrotomy in the knee	CPT-27310, CPT-27403, ICD-9-P-8016
Collateral and cruciate ligament repairs	CPT-27405, CPT-27407, CPT-27409
Extra-/intra-articular ligament reconstructions	CPT-27427, CPT-27428, CPT-27429
Knee dislocation surgery, open	CPT-27556, CPT-27557, CPT-27558

Appendix Table 2. Codes Used to Define Comorbidities Included in Demographic Factors

Comorbidity	Codes
Tobacco Use	ICD-9-D-3051, ICD-9-D-VI582, ICD-10-D-F17220, ICD-10-D-F17221, ICD-10-D-F17223, ICD-10-D-F17228, ICD-10-D-F17229, ICD-10-D-F17290, ICD-10-D-F17291, ICD-10-D-F17293, ICD-10-D-F17298, ICD-10-D-F17299, ICD-10-D-Z720
Diabetes	ICD-9-D-24900:ICD-9-D-25099,ICD-9-D-7902,ICD-9-D-79021,ICD-9-D-79022,ICD-9-D-79029, ICD-9-D-7915, ICD-9-D-7916, ICD-10-D-E090:ICD-10-D-E139
Obesity	ICD-9-D-2780, ICD-9-D-27800, ICD-9-D-27801, ICD-9-D-27802, ICD-9-D-27803, ICD-10-D-E660:ICD-10-D-E669