

Original Article

After Chondroplasty, Patient Election to Proceed With Cartilage Transplantation Is Closely and Additively Associated With Preoperative AMADEUS (Area Measurement And DEpth Underlying Structure) Grade, Condylar Involvement, Knee Injury and Osteoarthritis Outcome Score Pain Score, and Veterans Rand 12-Item Health Survey Physical Score

Adam B. Yanke, M.D., Ph.D., Mario Hevesi, M.D., Ph.D., Navya Dandu, M.D., Nicholas A. Trasolini, M.D., Reem Y. Darwish, B.S., Athan G. Zavras, M.D., and Brian J. Cole, M.D. M.B.A.

Purpose: To identify risk factors for patient election to proceed with cartilage transplant after staging chondroplasty. **Methods:** This study retrospectively reviewed patients prospectively enrolled at the time of staging chondroplasty, with early election defined as patient decision to proceed to cartilage transplantation within 6 months of chondroplasty. Cox proportional hazards analysis was used to determine univariate predictors of conversion, and a predictive calculator, the Cartilage Early Return for Transplant score, was formulated using stepwise regression employing the Akaike information criterion. Receiver operator curves and the area under the curve were used to evaluate the predictive ability of the final model on the studied patient population. **Results:** Sixty-five knees (63 patients) were evaluated, with an overall transplant election rate of 27.7% within 6 months after chondroplasty. Based on multivariate results, the final Akaike information criterion–driven Cartilage Early Return for Transplant score employed preoperative Knee Injury and Osteoarthritis Outcome Score Pain Score, Veterans Rand 12-Item Health Survey Physical Score, condylar involvement, and AMADEUS (Area Measurement And DEpth Underlying Structure) score to generate a 0- to 7-point risk-stratification system with a 3% early election to proceed to transplant risk in the 0- to 2-point score group, 33% risk in the 3- to 4-point group, and 79% risk in the 5+-point group ($P < .01$) and an overall AUC of 0.906 ($P < .01$). **Conclusions:** Risk of early patient election to pursue cartilage transplantation after chondroplasty is closely and additively associated with preoperative AMADEUS grade, condylar involvement, Knee Injury and Osteoarthritis Outcome Score Pain Score, and Veterans Rand 12-Item Health Survey Physical Score. **Clinical Relevance:** Understanding risk factors for conversion to cartilage transplantation may improve preoperative planning and counseling prior to staging chondroplasty.

From Rush University Medical Center, Chicago, Illinois, U.S.A.

A.B.Y. reports personal fees from CONMED Linvatec, personal fees from JRF Ortho, personal fees from Olympus, grants from Organogenesis, nonfinancial support and other from Patient IQ, nonfinancial support from Smith & Nephew, nonfinancial support from Sparta Biomedical, grants from Vericel, and grants from Arthrex, outside the submitted work. M.H. reports personal fees from Moximed, outside the submitted work. B.J.C. reports other from Aesculap, other from National Institutes of Health, other from Operative Techniques in Sports Medicine, personal fees from Ossio, personal fees and other from Regentis, other from Smith and Nephew, grants, personal fees and other from Arthrex, other from Elsevier publishing, other from Bandgrip, other from Acumed LLC, other from Encore Medical, LP, other from GE Healthcare, other from Merck Sharp & Dohme Corporation, other from

SportsTek Medical, and other from Vericel Corporation, outside the submitted work. Full ICMJE author disclosure forms are available for this article online, as [supplementary material](#).

Received October 5, 2021; revised manuscript received July 11, 2022; accepted July 13, 2022.

Address correspondence to Adam B. Yanke, M.D., Ph.D., 1611 W. Harrison St., St 300, Chicago, IL 60612. E-mail: Adam.yanke@rushortho.com

© 2022 Published by Elsevier Inc. on behalf of the Arthroscopy Association of North America. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

2666-061X/211394

<https://doi.org/10.1016/j.asmr.2022.07.005>

Articular cartilage injuries are common in a symptomatic knee, with chondral or osteochondral lesions noted in up to 69% of patients undergoing diagnostic knee arthroscopy.¹ Treatment of these articular cartilage lesions requires an algorithmic approach with consideration of bony alignment, concomitant meniscal pathology, patellofemoral or tibiofemoral stability, lesion size and location, lesion uni- versus bipolarity, and patient-specific physical demands.^{2,3} Management options are diverse due to the lack of a standard-of-care treatment.⁴ Significant clinical improvements have been reported with biologic injections,⁵ osteotomies,⁶⁻⁸ chondroplasty,⁹ marrow stimulation,^{10,11} autologous culture-expanded chondrocytes,^{12,13} particulated juvenile articular cartilage,¹⁴ osteochondral autograft transfer,¹⁵ and osteochondral allograft (OCA) transplantation.^{16,17}

While many of these procedures can be performed in a single stage, surgeons may elect to employ a staging chondroplasty to directly evaluate the size and location of chondral lesions, to debride unstable areas of articular cartilage, and to assess for concomitant and relevant pathology such as meniscus deficiency, apposing chondral surface status, and ligament status. Chondroplasty as a primary procedure for focal articular cartilage defects has demonstrated inconsistent results in the literature.^{9,18-21} Specifically, chondroplasty was not shown to provide symptomatic benefit as compared with observation alone in a randomized controlled trial,¹⁹ or provide significant benefit in delaying arthroplasty.¹⁸ However, other series have suggested that chondroplasty for articular cartilage defects less than 2 cm² and in the absence of concurrent meniscal pathology may be efficacious.^{9,21} Given the potential for meaningful clinical benefit and further informed decision-making following direct defect visualization, probing, and chondroplasty at the time of initial diagnostic arthroscopy, a single-stage definitive cartilage restoration procedure (OCA, minced cartilage allograft, etc.) may be found to be unnecessarily aggressive for certain patients.^{22,23}

To date, clinicians have insufficient data to determine which patients with full-thickness chondral defects will derive therapeutic and/or subsequent surgical planning benefit from an initial staging chondroplasty and which will not. Indeed, there may be cohorts of patients with particular preoperative clinical and imaging factors that predispose them to a poor outcome from initial chondroplasty or a high propensity to proceed with second-stage transplantation. In those patients, single-stage cartilage procedures may be considered. The purpose of this study was to identify risk factors for patient election to proceed with cartilage transplant after staging chondroplasty. We hypothesized that important factors would be the degree of preoperative

disability (as measured by patient-reported outcome scores), lesion location, topology, meniscal status, and lesion characteristics on magnetic resonance imaging (MRI).

Methods

After institutional review board approval (ORA 16081206), a retrospective analysis of a prospectively collected cartilage database was performed. Patients with symptoms and imaging findings consistent with focal cartilage defects of the knee were consented and prospectively enrolled into this clinical study before planned arthroscopic chondroplasty with 1 of 2 senior surgeons (A.B.Y. and B.J.C.).

Patients were included in this retrospective analysis if they consented to the prospective study, were considered adequate cartilage transplant candidates (specifically for OCA or autologous chondrocyte implantation), had a preoperative MRI available for review, and had a minimum of 6 months' follow-up for election to proceed with cartilage transplantation. Patients were excluded from this analysis if they were undergoing revision cartilage transplant procedures or were indicated for future ligament reconstructions, had large meniscal tears, were found to have extensive arthritis, or were considered for treatments other than cartilage transplant, such as arthroplasty or biologics (Appendix Table 1, available at www.arthroscopyjournal.org). Of note, patients were excluded from analysis if they were thought to be clearly indicated for a single-stage chondral procedure, such as may be the case for osteochondritis dissecans fragment refixation for large, nonfragmented lesions in young individuals or osteochondral allograft for patients with preoperative imaging clearly demonstrating a large (>2 cm²) single osteochondral defect in a weight-bearing location with clear subchondral/marrow involvement. In such a way, the study population was selected to be representative of cartilage patients in whom staging arthroscopy may provide both diagnostic and informed decision-making benefits.

For patients who underwent staging chondroplasty between 2017 and 2020, chart review was performed to determine age at time of chondroplasty, sex, body mass index (BMI), etiology of injury, and history of previous surgery. Indication for future meniscal allograft transplantation and indication for realignment procedure (high tibial osteotomy or distal femoral osteotomy) based on preoperative presentation and arthroscopic findings also were derived from chart review. Preoperative MRI was used to grade identifiable cartilage lesions according to the AMADEUS (Area Measurement And DEpth Underlying Structure) classification system, proposed by Jungmann et al.²⁴ The final AMADEUS grade (grade I [best, score >75] to grade IV [worst,

Table 1. Descriptive Characteristics of Chondral Pathology

Characteristic	Number (%)
Clinical history	
History of previous surgery	
Yes	35 (53.8%)
No	30 (46.2%)
Etiology	
Degenerative	41 (63.1%)
Traumatic	17 (26.2%)
Instability	7 (10.7%)
Defect locations	
Condylar involvement	
Present	34 (52.3%)
Absent	31 (47.7%)
Bipolar lesions	
Present	14 (21.5%)
Absent	51 (78.5%)
Multiple lesions	
Present	16 (24.6%)
Absent	49 (75.4%)
MRI characteristics	
Defect area, cm	2.4 ± 1.4
Defect depth	
Signal	5 (7.7%)
Partial	18 (27.7%)
Full	42 (64.6%)
Subchondral bone involvement	
Present	18 (27.7%)
Absent	47 (72.3%)
Bone marrow edema	
Present	33 (50.8%)
Absent	32 (49.2%)
AMADEUS score	58.5 ± 14.7
AMADEUS grade	
Grade 1	5 (7.7%)
Grade 2	36 (55.4%)
Grade 3	23 (35.4%)
Grade 4	1 (1.5%)

AMADEUS, Area Measurement And DEpth Underlying Structure; MRI, magnetic resonance imaging.

score <25]), as well as lesion location, number, bipolarity, bone marrow edema, and subchondral involvement were analyzed as risk factors. All measurements were made by one board-eligible orthopaedic surgeon (N.A.T.).

Outcome Measures

The primary outcome measure was the patient decision to proceed with cartilage transplant procedure within 6 months after initial arthroscopic chondroplasty based on continued symptoms, failure of conservative measures, or postoperative review of intraoperative findings prompting the patient to elect to the second stage treatment as part of a joint decision-making process. Due to the inherent variability in insurance authorization process, which could lead to delays in scheduling a surgical date for the transplant, this endpoint was standardized to the date at which the patient

elects to undergo further surgery, as dictated in a clinical note, and the insurance authorization process was initiated. This was considered to be a true postoperative decision and defined as the failure endpoint for analysis.

Analyses included predictive factors for conversion, including demographic data (age, sex, BMI), lesion etiology, lesion location, preoperative defect characteristics on MRI (lesion bipolarity, AMADEUS grade, bone marrow edema, subchondral involvement), concomitant meniscal deficiency (indication for meniscal allograft transplantation) or malalignment (indication for realignment osteotomy), and patient-reported functional assessment according to International Knee Documentation Committee (IKDC), Lysholm, Knee Injury and Osteoarthritis Outcome Score (KOOS), and Veterans Rand 12-Item Health Survey (VR-12 Mental and Physical) at baseline.

To corroborate patient symptoms with the decision to elect, a subanalysis of postoperative patient-reported outcomes was performed to (1) compare outcomes at 2 weeks and 6 weeks after chondroplasty between patients electing to proceed versus not electing to proceed to establish predictive thresholds for impending election and (2) examine trajectory of outcomes in patients not electing to proceed.

Statistical Analysis

Descriptive statistics were used to present demographic data with means, standard deviations, and percentages, as appropriate. Patients electing to proceed with cartilage transplant within 6 months of chondral debridement were compared with those completing at least 6 months of follow-up without electing to proceed to transplant. Cox proportional hazards analysis was used to determine univariate predictors of conversion.

A predictive scoring system was generated by entering all variables with univariate predictive value into a multivariable binary regression model. Subsequently, the ideal set of predictive variables was determined using stepwise regression employing the Akaike information criterion (AIC).²⁵ Using the AIC, goodness of fit could be quantified and optimized for univariate predictive variables while penalizing overfitted models that contain more parameters than justified by the data. This method was chosen to identify the variables with additively contribute to the final model while eliminating the univariate predictors which do not substantially contribute. Subsequently, receiver operator curves and the area under the curve (AUC) was used to evaluate the predictive ability of the Cartilage Early Return for Transplant (CERT) score on the studied patient population, as previously methodologies have described.²⁶ Testing was 2-sided, with $P < .05$ considered statistically significant. Analyses were conducted in R 4.0.0 (R Core Team, Vienna, Austria).

Table 2. Univariate Predictors of Early Failure of Therapeutic Chondroplasty

Variable	Hazards Ratio (95% CI)	P Value
Demographics		
Age, y	Reference	.77
<30	1.14 (0.47-2.81)	
≥30		
Sex	Reference	.70
Female	0.84 (0.36-1.99)	
Male		
BMI	Reference	.71
<30	1.21 (0.44-3.35)	
≥30		
History of previous surgery	Reference	.01
	3.83 (1.34-10.94)	
Preoperative imaging and surgical indications		
Defect location	Reference	.01
Patellofemoral	3.98 (1.37-11.61)	
Femoral condyles		
Number of lesions	Reference	<.01
Single	4.01 (1.62-9.95)	
Multiple		
Lesion topology	Reference	.03
Unipolar	2.74 (1.09-6.87)	
Bipolar		
Bone marrow edema	Reference	.83
Absent	0.91 (0.37-2.25)	
Edema present		
Subchondral involvement	Reference	.05
Absent	2.49 (1.00-6.20)	
Present		
AMADEUS grade	Reference	<.01
Grade 1	>.99	<.01
Grade 2	>.99	
Grade 3-4		
Lesion etiology	Reference	.18
Degenerative (OA)	1.90 (0.74-4.90)	.88
Traumatic	1.12 (0.26-4.72)	
Instability		
Concurrent indication for MAT	1.19 (0.46-3.03)	.72
Concurrent indication for realignment procedure	Reference	.013
	3.94 (1.33-11.68)	
Preoperative outcome scores		
IKDC	0.96 (0.93-0.99)	.02
KOOS	0.98 (0.95-1.00)	.06
Symptoms	0.97 (0.95-0.99)	.01
Pain	0.97 (0.94-0.99)	.02
ADL	0.99 (0.96-1.02)	.51
Sports	0.96 (0.92-1.00)	.07
Quality of life	0.96 (0.93-0.99)	.01
Joint replacement		
Lysholm	0.98 (0.95-1.00)	.08
VR-12	0.95 (0.91-0.98)	<.01
Mental Health	0.92 (0.86-1.00)	.04
Physical Health		

AMADEUS, Area Measurement and DEpth Underlying Structure; ADL, activities of daily living; CI, confidence interval; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; MAT, meniscal allograft transplantation; OA, osteoarthritis; VR-12, Veterans Rand 12-Item Health Survey.

Results

A total of 120 patients (122 knees) were prospectively enrolled, and 80 knees met inclusion criteria for the study ([Appendix Table 1](#), available at www.arthroscopyjournal.org). Thirteen patients were lost to follow-up, and 2 patients did not have preoperative MRI available for review. A final cohort of 65 arthroscopic chondroplasties performed between May 2017 and June 2020 in 63 patients (35 male, 30 female) were analyzed. Mean age was 32.6 ± 8.5 years and mean BMI was 27.7 ± 5.7 . Patients were followed for a mean of 14.1 ± 7.4 months (range 6.0-36.1). All excluded patients were similar in age (34.40 ± 9.62 vs 32.69 ± 8.66 , $P = .305$) and sex (52.70% vs 55.38% male, $P = .783$) compared with included patients. However, excluded patients had a slightly greater BMI than included patients (30.30 ± 6.63 vs 27.81 ± 5.70 , $P = .029$). Descriptive characteristics of the chondral pathologies are presented in [Table 1](#).

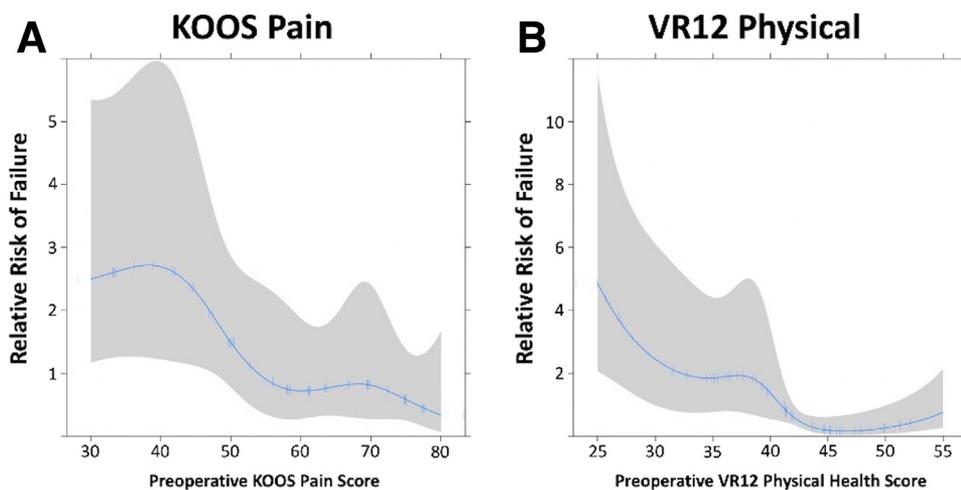
Preoperative Risk Factors for Failure of Chondroplasty

During the course of follow-up, 18 patients (18/65 knees, 27.7%) elected to proceed with cartilage transplantation within 6 months of chondroplasty, with the decision occurring at an average of 2.0 ± 1.5 months (range 0.2-4.8) following their index surgery. Significant differences were observed on univariate Cox proportional hazards analysis between early conversion patients and controls for femoral condyle defect location, bipolar and multiple lesions, subchondral involvement, AMADEUS grade, as well as preoperative IKDC score, KOOS pain, activities of daily living (ADL), and joint replacement score, and VR-12 Mental and Physical Health Score ([Table 2](#)). History of previous surgery (hazard ratio 3.83, 95% confidence interval 1.34-10.94, $P = .01$) and indication for realignment procedure (hazard ratio 3.94, 95% confidence interval 1.33-11.68, $P = .013$) were also significant on univariate analysis. However, they become nonsignificant on multivariate analysis. Ultimately, 16 of 18 patients who elected to proceed underwent cartilage transplantation.

Development of a Preoperative Risk Calculator

Multivariable analysis for predictors of early conversion to cartilage transplant was performed employing stepwise regression with the AIC and assessment of the relative risk represented by each predictive factor. Femoral condyle involvement was determined to be a significant predictor of early conversion to transplantation in the final model, along with KOOS Pain score, VR-12 Physical Score, and AMADEUS score 3 to 4. When we examined the risk relationship between

Fig 1. Relative risk of failure and conversion to cartilage transplantation by preoperative (A) KOOS Pain score, and (B) VR-12 Physical Health score. Shaded area represents 95% confidence interval. (KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veterans Rand 12-Item Health Survey.)



KOOS Pain and VR-12 Physical Score and election to proceed with transplant, patients with respective preoperative scores <40 were found to demonstrate substantially greater risk of failure ($P = .04$ and $.02$, respectively) than patients with scores ≥ 40 , as demonstrated in Fig 1 A and B.

Normalization of the relative contributions of each the 4 variables in the AIC-driven final model generated a readily employable preoperative scoring system, the CERT score (Table 3). CERT scores were calculated and applied to our dataset to determine its prognostic value. Post hoc analysis determining the ability of the CERT score to stratify patient's transplantation was then performed. Patients with increasing CERT scores demonstrated increased rates of election of cartilage transplantation, with a 3% risk in the 0- to 2-point score group, 33% risk in the 3- to 4-point group, and 79% risk in the 5+-point group ($P < .01$). To further quantify CERT score performance, the receiver-operating characteristics of the CERT score and its associated AUC were generated (Fig 2). The CERT score was determined to have satisfactory and statistically significant AUC of 0.906 ($P < .01$).

Comparison of Patient-Reported Outcomes Between Patients Electing or Not Electing to Proceed

Patient-reported outcome questionnaires were completed at 2 weeks' and 6 weeks' postchondroplasty by 58.21% and 74.63% of patients. At 2 weeks, early-electing patients demonstrated lower functional scores for KOOS Pain (51.49 ± 19.26 vs 68.37 ± 17.41 , $P = .01$), KOOS ADL (72.92 ± 19.10 vs 57.01 ± 21.07 , $P = .03$), and KOOS Quality of Life (40.52 ± 19.87 vs 17.79 ± 14.84 , $P = .001$). By 6 weeks, early electing patients demonstrated significantly worse pain (61.71 ± 17.97 vs 77.03 ± 14.79 , $P = .003$), daily living (84.75 ± 14.26 vs 67.55 ± 20.69 , $P = .002$), sports (57.36

± 22.94 vs 32.14 ± 28.67 , $P = .002$), and quality of life scores (49.31 ± 21.27 vs 22.33 ± 20.33 , $P < .001$).

Analysis of Patients Not Electing to Proceed With Transplant by 6 Months

Forty-five patients (47 knees) in the overall cohort did not elect to proceed with cartilage transplantation within 6 months. Three patients eventually elected to proceed to cartilage transplant procedure at a mean of 1.32 ± 0.30 years after chondroplasty. One patient suffered an acute patellar tendon rupture 8 months after chondroplasty, so outcomes after the 6-month timepoint were not included for analysis.

Mean postoperative outcomes significantly improved from baseline to 2 weeks for KOOS Symptoms (56.08 ± 17.41 to 62.58 ± 16.31 , $P = .039$), KOOS Pain (61.32 ± 20.12 to 68.37 ± 17.41 , $P = .040$), and KOOS Quality of Life (32.25 ± 17.18 to 40.52 ± 19.87 , $P = .031$). All baseline scores significantly improved by

Table 3. Early Cartilage Transplant Score Calculation

Risk Factor	Point Value
Defect location	0
Patellofemoral	2
Femoral condyles	
KOOS Pain	0
≥ 40	2
< 40	
VR-12 physical score	0
≥ 40	2
< 40	
AMADEUS score*	0
1-2	1
3-4	
Total:	0-7 points

AMADEUS, Area Measurement And DEpth Underlying Structure; KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veterans Rand 12-Item Health Survey.

*Lesion with greatest score in case of multiple lesions.

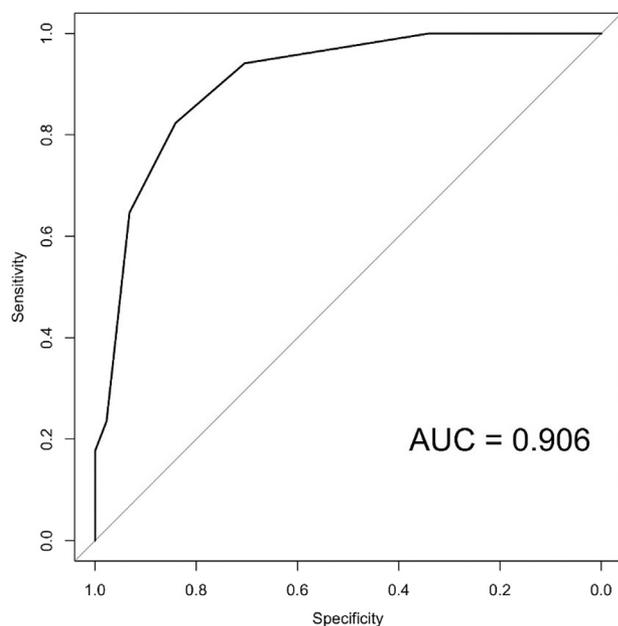


Fig 2. ROC curve for the study data. (AUC, area under the curve; ROC, receiver operating characteristic.)

6 weeks for KOOS Symptoms (72.12 ± 13.92 , $P < .001$), KOOS Pain (77.03 ± 14.79 , $P < .001$), KOOS ADL (73.96 ± 17.19 to 84.75 ± 14.26 , $P < .001$), KOOS Sports (35.97 ± 16.77 to 57.36 ± 22.94 , $P < .001$), and Quality of Life (49.31 ± 21.27 , $P < .001$). At 6 months and 1 year, 64.44% and 57.78% of patients, respectively, completed questionnaires. All scores were significantly greater at 6 months, for IKDC (42.10 ± 12.77 to 63.64 ± 16.47 , $P < .001$), KOOS Symptoms (74.28 ± 13.83 , $P < .001$), KOOS Pain (78.55 ± 15.03 , $P < .001$), KOOS ADL (87.17 ± 16.83 , $P < .001$), KOOS Sports (59.00 ± 21.65 , $P < .001$), and KOOS Quality of Life (51.00 ± 23.98 , $P < .001$). All postoperative scores at 1 year were also significantly greater than baseline scores for IKDC (66.45 ± 19.62 , $P < .001$), KOOS Symptoms (75.29 ± 18.32 , $P < .001$), KOOS Pain (78.67 ± 15.99 , $P < .001$), KOOS ADL (86.77 ± 17.04 , $P = .013$), KOOS Sports (61.20 ± 24.68 , $P < .001$), and KOOS Quality of Life (55.01 ± 23.59 , $P < .001$).

Discussion

This study identified several preoperative risk factors that were predictive of early patient election to proceed with cartilage transplantation procedures after staging chondroplasty, which additively formed a risk calculator—condylar involvement, defect AMADEUS grade of 3 to 4 on preoperative MRI, KOOS Pain Score <40 , and VR-12 Physical Score <40 . Overall, early election was a relatively common occurrence, with 27.7% of patients electing for transplantation before 6 months.

When an early decision to proceed to transplant occurred, it did so at a mean of 2.0 months status postchondroplasty, with the earliest decision made within the first postoperative week. Of note, such early decision-making was based on joint decision-making with the patient following review of arthroscopic findings as well as continued postoperative dissatisfaction with symptomatic state. Understandably, patients with large condylar defects noted intraoperatively and high pre- and postoperative pain scores may wish to convert early to second stage planning as not to extend overall recovery timeline rather than following a prolonged “wait-and-see” approach in light of substantial visualized intra-articular pathology and associated disability.

While several variables that are traditionally taken into consideration during the surgical decision-making process (e.g., alignment, lesion topology) were significant on univariate analysis, only the selected variables (AMADEUS grade, condylar involvement, KOOS Pain Score, and VR-12 Physical Score) independently and additively contributed to the final model and were therefore the only ones included in the calculator. These findings are further supported by the subanalysis of patient-reported outcomes, which demonstrated that patients electing to proceed with cartilage transplantation reported worse outcomes at 6 weeks (which was approximately the mean time to decision) compared with patients not electing to proceed. Therefore, while the decision to proceed with transplantation may be a shared decision by surgeon and patient, it was driven by severity of patient symptoms. Patients who did not elect to proceed within 6 months demonstrated significant improvements from baseline out to 1 year postchondroplasty, demonstrating some sustained therapeutic benefit of chondroplasty.

The finding that severe AMADEUS grade significantly predicted early conversion provides additional evidence for its use as a metric for presurgical planning. It was designed specifically as a preoperative score to address deficiencies in existing MRI-based classification systems that failed to incorporate several pathologic components that typically guide management decisions (e.g., lesion size).^{24,27,28} The individual components of the scoring system have been shown to have high inter-rater reliability, with the lowest interclass correlation coefficient being 0.63 for defect depth grading and all others in the range of 0.8 to 0.9, making it a valuable option for preoperative staging of cartilage lesions.²⁴ Previous studies that investigated its clinical utility demonstrated a moderate correlation with the Core Outcome Measures Index preoperatively for patients undergoing matrix-associated autochondrocyte implantation, indicating that its major components capture the specific parameters which directly correlate with the patient's pathology.²⁹ The results of the present study therefore further demonstrate the utility of

the AMADEUS system for assessing a patient's response to chondroplasty and planning for potential future surgical procedures when considered in the context of the other additive calculator factors, including patient symptoms and defect location.

Additional preoperative MRI factors that were significant on univariate analysis included lesion bipolarity and number of lesions. While these factors may influence surgical decision-making, they were found in multivariate statistical analysis to not independently contribute sufficiently on stepwise regression analysis to factor into the CERT scoring system. The characteristics of the most severe lesion and its location had a greater impact on the decision to return for early cartilage transplant. It is possible that bipolarity and number of lesions contribute to preoperative KOOS Pain and VR-12 Physical Score, but this potential confounding effect requires further study. In addition, indication for realignment procedure was significant on univariate analysis, but became nonsignificant on multivariate analysis. This finding is aligned with the expert consensus in that malalignment is among several important factors that are necessary to assess and address either before or in conjunction with cartilage transplantation.³⁰ Our study suggests that although indication for a realignment procedure correlates independently with subsequently proceeding with a second stage procedure, election to proceed is better predicted by a constellation of other variables involving anatomic location, defect grade, and patient function. Similarly, history of previous surgery was also significant on univariate analysis, but became nonsignificant on multivariate analysis. As this cohort was heterogeneous in types of previous surgery (e.g., anterior cruciate ligament vs previous arthroscopy), and sample size was insufficient for subanalysis, the specific effects of cartilage versus noncartilage-related previous surgery could not be assessed. Future studies are required to define a specific threshold for concerning malalignment and to investigate the role of previous cartilage versus noncartilage-related previous surgery.

The finding that worse preoperative pain and function scores predict early reoperation was expected in this study and is consistent with literature demonstrating that pain and related psychological tendencies are associated with poorer outcomes.³¹ Patients with worse preoperative function may need more aggressive interventions to return to an acceptable level of function. In contrast to this, Anderson et al.⁹ found that patients with lower preoperative PROs demonstrated larger improvements after chondroplasty for articular cartilage defects of the knee. In their cohort of patients with isolated chondral pathology, only 15% of patients underwent subsequent surgery within the follow-up period. The greater rate cited by our study may potentially be attributed to the inclusion of patients

with additional pathologies such as meniscal deficiency or malalignment, which was not reported by authors of the aforementioned study. Another differentiating factor is the absence of threshold analysis to determine factors related to outcome failure. Without threshold analysis for outcome, it is difficult to directly correlate these findings to the results of our study. Further prospective application of the CERT score should be performed to test its prognostic ability and clarify its external validity.

The univariate risk factor analysis was useful in identifying factors that were not significant predictors of early conversion to cartilage transplant. Patient age, sex, and BMI were not predictors of early conversion. Similarly, lesion etiology did not have a significant impact on early failure of chondroplasty. These results align with previous studies, such as that of 54 chondroplasties in professional athletes, which found no effect of lesion size or patient age on return to sport rates.³² Although these factors may not predict early conversion, they should remain a part of the surgical treatment algorithm for chondral lesions and retain a critical role in surgical planning for definitive cartilage restoration.³⁰

There are clinical applications of this study. First, decisions regarding 1-stage versus 2-stage cartilage treatment can be challenging. While single-stage treatments are appealing, staging arthroscopy has been shown to change the definitive surgical plan in 36.7% of cases.²³ In addition, chondroplasty performed at the staging procedure may lead to symptomatic improvements.⁹ Unfortunately, the benefit of chondroplasty is not universal; in the present study, 29.9% of patients did not benefit and elected to proceed with subsequent surgical treatment by 6 months postoperatively. This could be due in part to patient selection, which could potentially be improved with implementation of the risk calculator designed by this study.

Limitations

There are several limitations to this retrospective analysis of prospectively collected data. While sample size was adequate for the statistical comparisons and the creation of a statistically significant risk calculator, a larger sample size would further improve statistical power and fine-tune stratification between each individual CERT subscore. This applies also the subscore addition of other variables to the CERT scores. While our post hoc receiver operating characteristic curves and stratification testing yielded statistically significant results for the CERT score's stratification value ($P < .01$) and sensitivity / specificity ($P < .01$), increased sample sizes would allow for subregression of additional variables, understanding that models ideally contain approximately 10 events per predictive variable, particularly as it relates to simulation methods, but a

lower number of events per variable (5 in our presented analysis) may provide the significant results observed, particularly if there is substantial separation amongst groups, such as was the case in our data as well as the discriminant analysis investigation performed with 3 subjects per group by Lachenbruch and Goldstein.³³⁻³⁵ While previous studies, like ours, have published an AUC tested on the same cohort as the originating study, future efforts of external validation in a different patient population will be necessary to demonstrate broad generalizability and applicability of this and other clinical scores. Larger sample size would also allow further exploration of history of previous surgery, as this was a heterogenous variable in the current sample. Further investigation will be needed to evaluate the potential effects of previous noncartilage-related procedures (e.g., ACL) versus previous arthroscopy. Many patients also were excluded based on a priori criteria. While there were no clear demographic differences in the excluded cohort aside from BMI, there remains the possibility of selection bias. Furthermore, patients with 2 affected knees would generally choose one knee to treat first, if electing to proceed at all. However, our failure (i.e., decision to proceed to a second stage) cohort did not include any patients with bilateral pathology, and therefore this variable did not play a confounding role in the presented series and was not included in analyses. In addition, as indication for realignment procedure was collected retrospectively, not all patients within this cohort had mechanical axis views to measure coronal alignment. Therefore, although it was significant on univariate, alignment will require further exploration and we could not draw adequate conclusions from this study. Finally, this was a study of early treatment failure and reoperation. It was limited in its minimum duration of follow-up of only 6 months. While the follow-up period was sufficient for the study to address its purpose of defining risk factors for early conversion to cartilage transplant, it did not evaluate the longer-term benefits of staging chondroplasty and did not define reoperation rates at later time points. The outcomes of cartilage transplantation were also not assessed, and therefore the final status of patients electing to proceed cannot be commented upon. Furthermore, the clinical utility of the CERT score may be limited for surgeons who primarily opt for 2-stage procedures (e.g., autochondrocyte implantation). However, it would still allow for evidence-based discussion about expected therapeutic benefit from chondroplasty with the patient. Lastly, this study design was subject to bias. Specifically, the exclusion criteria (e.g., large meniscal tears), while employed to identify a more homogenous cohort, may increase the risk of selection bias. Similarly, the endpoint of election to proceed, while chosen to eliminate issues with insurance-related delays, is subject to cognitive and

presentation bias from operative counseling in the shared decision-making model.^{36,37}

Conclusions

Risk of early patient election to pursue cartilage transplantation after chondroplasty is closely and additively associated with preoperative AMADEUS grade, condylar involvement, KOOS Pain Score, and VR-12 Physical Score.

References

1. Fodor P, Sólyom Á, Fodor R, Ivănescu A, Băţagă T. Prevalence of chondral lesions in knee arthroscopy. *J Interdisciplinary Med* 2018;3:21-24.
2. Krych AJ, Saris DBF, Stuart MJ, Hacken B. Cartilage injury in the knee: Assessment and treatment options. *J Am Acad Orthop Surg* 2020;28:914-922.
3. Weber AE, Gitelis ME, McCarthy MA, Yanke AB, Cole BJ. Malalignment: A requirement for cartilage and organ restoration. *Sports Med Arthrosc Rev* 2016;24:e14-e22.
4. Devitt BM, Bell SW, Webster KE, Feller JA, Whitehead TS. Surgical treatments of cartilage defects of the knee: Systematic review of randomised controlled trials. *Knee* 2017;24:508-517.
5. Arshi A, Petrigliano FA, Williams RJ, Jones KJ. Stem cell treatment for knee articular cartilage defects and osteoarthritis. *Curr Rev Musculoskelet Med* 2020;13:20-27.
6. Klinge SA, Fulkerson JP. Fifteen-year minimum follow-up of anteromedial tibial tubercle transfer for lateral and/or distal patellofemoral arthrosis. *Arthroscopy* 2019;35:2146-2151.
7. Harris JD, Hussey K, Saltzman BM, et al. Cartilage repair with or without meniscal transplantation and osteotomy for lateral compartment chondral defects of the knee: Case series with minimum 2-year follow-up. *Orthop J Sports Med* 2014;2:2325967114551528.
8. Ollivier B, Berger P, Depuydt C, Vandenneucker H. Good long-term survival and patient-reported outcomes after high tibial osteotomy for medial compartment osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2021;29:3569-3584.
9. Anderson DE, Rose MB, Wille AJ, Wiedrick J, Crawford DC. Arthroscopic mechanical chondroplasty of the knee is beneficial for treatment of focal cartilage lesions in the absence of concurrent pathology. *Orthop J Sports Med* 2017;5:232596711770721.
10. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee: Average 11-year follow-up. *Arthroscopy* 2003;19:477-484.
11. Benthien JP, Behrens P. Nanofractured autologous matrix induced chondrogenesis (NAMIC®)—Further development of collagen membrane aided chondrogenesis combined with subchondral needling. *Knee* 2015;22:411-415.
12. Ebert JR, Fallon M, Ackland TR, Janes GC, Wood DJ. Minimum 10-year clinical and radiological outcomes of a randomized controlled trial evaluating 2 different approaches to full weightbearing after matrix-induced autologous chondrocyte implantation. *Am J Sports Med* 2020;48:133-142.

13. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med* 1994;331:889-895.
14. Farr J, Tabet SK, Margerrison E, Cole BJ. Clinical, radiographic, and histological outcomes after cartilage repair with particulated juvenile articular cartilage: A 2-year prospective study. *Am J Sports Med* 2014;42:1417-1425.
15. Solheim E, Hegna J, Strand T, Harlem T, Inderhaug E. Randomized study of long-term (15-17 years) outcome after microfracture versus mosaicplasty in knee articular cartilage defects. *Am J Sports Med* 2018;46:826-831.
16. Williams RJ, Ranawat AS, Potter HG, Carter T, Warren RF. Fresh stored allografts for the treatment of osteochondral defects of the knee. *J Bone Joint Surg* 2007;89:718-726.
17. LaPrade RF, Botker J, Herzog M, Agel J. Refrigerated osteoarticular allografts to treat articular cartilage defects of the femoral condyles. *J Bone Joint Surg Am* 2009;91:805-811.
18. Abram SGF, Palmer AJR, Judge A, Beard DJ, Price AJ. Rates of knee arthroplasty in patients with a history of arthroscopic chondroplasty: Results from a retrospective cohort study utilising the National Hospital Episode Statistics for England. *BMJ Open* 2020;10:e030609.
19. Bisson LJ, Kluczynski MA, Wind WM, et al. Patient outcomes after observation versus debridement of unstable chondral lesions during partial meniscectomy. *J Bone Joint Surg* 2017;99:1078-1085.
20. Spahn G, Hofmann GO, Von Engelhardt LV. Mechanical debridement versus radiofrequency in knee chondroplasty with concomitant medial meniscectomy: 10-year results from a randomized controlled study. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1560-1568.
21. Weißenberger M, Heinz T, Boelch SP, et al. Is debridement beneficial for focal cartilage defects of the knee: Data from the German Cartilage Registry (KnorpelRegister DGOU). *Arch Orthop Trauma Surg* 2020;140:373-382.
22. Christian DR, Oliver-Welsh L, Yanke AB, Cole BJ. Staging and practical issues in complex cases. Basel, Switzerland: Springer International Publishing, 2018;119-130.
23. Salem HS, Chaudhry ZS, Lucenti L, Tucker BS, Freedman KB. The importance of staging arthroscopy for chondral defects of the knee. *J Knee Surg* 2022;35:145-149.
24. Jungmann PM, Welsch GH, Brittberg M, et al. Magnetic Resonance Imaging Score and Classification System (AMADEUS) for assessment of preoperative cartilage defect severity. *Cartilage* 2017;8:272-282.
25. Akaike H. Information theory and an extension of the maximum likelihood principle. New York. In: Parzen E, Tanabe K, Kitagawa G, eds. *Selected papers of Hirotugu Akaike*. New York: Springer, 1998;199-213.
26. Hevesi M, Heidenreich MJ, Camp CL, et al. The recurrent instability of the patella score: A statistically based model for prediction of long-term recurrence risk after first-time dislocation. *Arthroscopy* 2019;35:537-543.
27. Alizai H, Virayavanich W, Joseph GB, et al. Cartilage lesion score: Comparison of a quantitative assessment score with established semiquantitative MR scoring systems. *Radiology* 2014;271:479-487.
28. Yulish BS, Montanez J, Goodfellow DB, Bryan PJ, Mulopulos GP, Modic MT. Chondromalacia patellae: Assessment with MR imaging. *Radiology* 1987;164:763-766.
29. Runer A, Jungmann P, Welsch G, et al. Correlation between the AMADEUS score and preoperative clinical patient-reported outcome measurements (PROMs) in patients undergoing matrix-induced autologous chondrocyte implantation (MACI). *J Orthop Surg Res* 2019;14:87.
30. Chahla J, Hinckel BB, Yanke AB, et al. An expert consensus statement on the management of large chondral and osteochondral defects in the patellofemoral joint. *Orthop J Sports Med* 2020;8:232596712090734.
31. Thompson K, Kramarchuk M, Yagnatovsky M, et al. Pain catastrophizing is associated with increased physical disability in patients with anterior knee pain. *J Orthop* 2020;21:283-286.
32. Scillia AJ, Aune KT, Andrachuk JS, et al. Return to play after chondroplasty of the knee in National Football League athletes. *Am J Sports Med* 2015;43:663-668.
33. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-1379.
34. Austin PC, Steyerberg EW. Events per variable (EPV) and the relative performance of different strategies for estimating the out-of-sample validity of logistic regression models. *Stat Methods Med Res* 2017;26:796-808.
35. Lachenbruch PA, Goldstein M. Discriminant analysis. *Biometrics* 1979;69-85.
36. Ozdemir S, Finkelstein EA. Cognitive bias: The downside of shared decision making. *JCO Clin Cancer Inform* 2018;2:1-10.
37. Loewenstein G, Brennan T, Volpp KG. Asymmetric paternalism to improve health behaviors. *JAMA* 2007;298:2415-2417.

Appendix Table 1. Patients Meeting Exclusion Criteria

Exclusion Criteria	N
Not considered adequate transplant candidate or other procedures recommended (biologics)	13
Extensive osteoarthritis, arthroplasty candidates	11
Large meniscal tears noted at debridement	6
Indication for concomitant ACLR	5
Complicated patellar instability or indication for MPFLR	5
Revision cartilage procedure	2
Lost to follow-up	13
No preoperative MRI	2

ACLR, anterior cruciate ligament reconstruction; MPFLR, medial patellofemoral ligament reconstruction; MRI, magnetic resonance imaging.