Published in final edited form as:

Am J Sports Med. 2018 March ; 46(4): 876–882. doi:10.1177/0363546517751139.

Differences in Lateral Compartment Joint Space Width after ACL Reconstruction: Data from the MOON Onsite Cohort

MOON Knee Group

Abstract

Background—Anterior cruciate ligament reconstruction (ACLR) can effectively return athletes to the playing field, but they are still at risk of developing post-traumatic osteoarthritis (PTOA). No studies have used multivariable analysis to evaluate the predictors of radiographic PTOA in the lateral compartment of the knee at short term follow-up after ACLR.

Purpose—To determine the predictors of radiographic joint space narrowing in the lateral compartment 2–3 years after ACLR in a young, active cohort.

Study Design—Cohort study.

Methods—A nested cohort of 358 patients from the Multicenter Orthopaedic Outcomes Network (MOON) prospective cohort who were 35 or younger, were injured playing a sport, and had never

Corresponding Author: Morgan H. Jones, MD, MPH, Orthopaedic and Rheumatologic Institute, Cleveland Clinic, 5555 Transportation Blvd., Garfield Heights, OH 44125, jonesm7@ccf.org.

Contributing authors of the MOON Knee Group:

Morgan H. Jones, MD, MPH¹

Kurt P. Spindler, MD¹

Jack T. Andrich, MD¹

Charles L. Cox, MD, MPH²

Warren R. Dunn, MD, MPH³

Jeff Duryea, PhD⁴

Carol L. Duong²

David C. Flanigan, MD⁵

Braden C. Fleming, PhD⁶

Laura J. Huston, MS²

Christopher C. Kaeding, MD⁵

Matthew J. Matava, MD⁷

Nancy A. Obuchowski, PhD⁸

Heidi L. Oksendahl, MSPT⁹

Richard D. Parker, MD¹

Erica A. Scaramuzza²

Matthew V. Smith, MD⁷

Carl S. Winalski, MD^{10,11}

Rick W. Wright, MD⁷

Emily K. Reinke, PhD²

¹Orthopaedic and Rheumatologic Institute, Cleveland Clinic, Cleveland, OH

²Department of Orthopaedic Surgery and Rehabilitation, Vanderbilt University Medical Center, Nashville, TN

³Department of Orthopaedics, Reedsburg Area Medical Center, Reedsburg, WI

⁴Department of Radiology, Brigham and Women's Hospital/Harvard Medical School, Boston, MA

⁵Department of Orthopaedics, The Ohio State University Wexner Medical Center, Columbus, OH

⁶Department of Orthopaedics, Warren Alpert Medical School of Brown University/Rhode Island Hospital, Providence, RI

⁷Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, MO

⁸Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH

⁹Steamboat Physical Therapy, Olympia, WA

¹⁰Section of Musculoskeletal Imaging, Imaging Institute, Cleveland Clinic, Cleveland, OH

¹¹Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, OH

Investigation performed at Cleveland Clinic, Cleveland, Ohio and Vanderbilt University Medical Center, Nashville, Tennessee, USA

had surgery on the contralateral knee were followed up two years after ACLR with questionnaires and with weight bearing knee radiographs using the metatarsophalangeal joint (MTP) technique. Joint space width in the lateral compartment was measured using a semiautomatic computerized method and multivariable predictive modeling was used to evaluate the relationship between meniscus treatment, cartilage injury, graft choice, and joint space while adjusting for age, sex, BMI and Marx activity level.

Results—Lateral joint space width was 0.11 mm narrower on the ACL reconstructed knees compared to the contralateral normal knees (7.69 mm vs. 7.80 mm, $p<0.01$). Statistically significant predictors of narrower joint space width on the ACL reconstructed side included lateral meniscectomy ($p<0.001$) and Marx activity level less than 16 ($p<0.001$).

Conclusion—This study identifies lateral meniscectomy and lower baseline Marx activity level to be predictors of radiographic joint space narrowing in the lateral compartment 2–3 years after ACLR in young, active patients without prior knee injury.

Clinical Relevance—Knowledge of the predictors of radiographic PTOA after ACLR provides useful information for clinicians to use when counseling their patients, and also can help to guide future research by investigators studying ways to prevent the progression of PTOA.

Keywords

meniscus; post-traumatic osteoarthritis; anterior cruciate ligament; imaging and radiology

Introduction

Anterior cruciate ligament (ACL) reconstruction can consistently improve knee stability and return recreational and competitive athletes to their sports, but these patients are still at risk of developing post-traumatic osteoarthritis (OA).⁴ Short term follow-up with MRI has demonstrated cartilage changes as early as 6 months post-operatively,¹⁶ but hasn't stratified based on meniscus pathology due to small sample size. A systematic review of longer term radiographic studies at 10 – 20 years post-surgery has demonstrated radiographic signs of OA in up to 50 percent of subjects with worse radiographic change in ACL reconstruction patients who have a meniscus tear;¹⁰ however, no short term studies with radiographic outcomes have had sufficient sample size to determine predictors of early radiographic change.

We have used a novel nested cohort within the larger Multicenter Orthopaedic Outcomes Network (MOON) prospective cohort to evaluate the initiation, progression and risk factors for post-traumatic OA. The subjects were less than 35 years of age, were injured in sports, and had never undergone contralateral knee surgery. The nested cohort was restricted to subjects who were injured playing a sport because we wanted to exclude patients with extremely high- or low-energy injuries and examine the development of post-traumatic OA after ACL reconstruction in the injured athlete. We showed that meniscus repair, partial meniscectomy and older age were associated with narrower medial compartment joint space 2–3 years post-operatively.⁸

The goal of the current project was to utilize the same nested cohort of young, active individuals to determine the baseline factors associated with narrower lateral compartment joint space width at the same time point 2–3 years after ACL reconstruction. We hypothesized that lateral meniscectomy and cartilage lesions in the lateral compartment would be associated with narrower lateral joint space.

Materials and Methods

Subjects

Subjects were recruited from the (MOON) prospective cohort of 869 eligible patients who underwent ACL reconstruction from 2005–2012. This study was approved by the Institutional Review Board at the coordinating center and at each participating site; subjects completed informed consent prior to enrollment. Only skeletally mature or nearly skeletally mature patients were included in the cohort; patients who underwent pediatric ACL reconstructions were excluded. All subjects completed questionnaires at enrollment and at the 2-year follow-up to capture demographic variables and patient reported outcome measures including Marx activity level.⁹ Surgeons completed questionnaires at the time of surgery to document physical examination, arthroscopic findings, and details of surgical technique including graft choice and meniscus treatment. Meniscus treatment was classified as normal meniscus (no treatment), meniscus tear stable to probing and central to popliteal hiatus (untreated tear), meniscal repair, or partial meniscectomy. Cartilage was classified as normal/grade 1 or grade 2, 3, or 4. Subjects were eligible for enrollment in the nested cohort if they had surgery by one of five senior surgeons (JTA, CCK, RDP, KPS, RWW), were 35 or younger at the time of follow-up, were injured while playing a sport, had no concomitant MCL, LCL, or PCL surgery, and had no history of ACL revision or contralateral knee surgery. Patients were still included in the study if they had a MCL injury that did not require repair. Subjects returned to their enrollment site for follow-up, including radiographs between 2 and 3.3 years post-operatively.

Radiographic Technique

The metatarsophalangeal (MTP) radiographic technique was used. Subjects were positioned with the first MTP joint directly underneath the front of the x-ray detector with their feet in 15 degrees of external rotation.¹¹ They bent their knees so that the patella touched the detector. Consistency of positioning was achieved by using identical positioning equipment at all sites. A free-standing reference containing balls that were 5 mm in diameter and spaced 10 mm apart (Radiation Product Design, Albertville, MN) was utilized to allow calibration for differences in magnification. The reference standard was placed next to the fibular head, vertical to the ground. Each knee was imaged individually using a variety of radiographic equipment (site dependent) including Siemens Polyphos (Siemens, Tarrytown, NY) and Shimadzu RADspeed machines (Shimadzu, Nakagyo-ku, Kyoto, Japan) using AGFA CR cassettes (Agfa HealthCare, Greenville, SC) as well as GE De fi nium (GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom), Hologic DR (Hologic, Bedford, MA) and Fuji FDX 6.2 (FUJIFILM Medical Systems Stamford, CT) digital machines. Exposure was adjusted to achieve optimal image quality, and all radiologic technologists were trained in subject positioning by the study coordinator from the

coordinating center prior to beginning the study. For some images, YAKAMI DICOM Tools (Masahiro Yakami, Department of Diagnostic Imaging and Nuclear Medicine, Kyoto University, Kyoto, Japan) were employed to remove identifiers and prepare images for analysis.

Radiographic Joint Space Width Measurement

Multiple steps were taken to de-identify images and prepare them for analysis: XnView open-source image processing software (XnSoft, La Neuville, Reims, France) was used to convert images to TIFF format to erase all metadata; images were then converted back to compressed DICOM format using Adobe Photoshop CS6 (Adobe Systems Inc., San Jose, CA). OsiriX open source DICOM viewer software (www.osirix-viewer.com) was used to convert compressed DICOM images to uncompressed DICOM images for analysis.

Radiographic joint space width was measured using a previously described semi-automated computerized method that delineates the tibial and femoral joint surfaces and measures the joint space width at a fixed location 72.5% of the distance from the medial edge to the lateral edge of the tibia.⁵ This location was found to be highly sensitive for detecting progression of lateral joint space width changes in data from the Osteoarthritis Initiative (OAI).⁷ Individuals were removed from the analysis if they did not have a valid measure at this point. The reader was blinded to patient demographics and treatment status, and images were evaluated with the reader viewing the left and right knee simultaneously.

Images were excluded when the following two technical factors raised concern about the reliability of the joint space width measurement value. First, images were excluded if the reader judged there to be indistinct lateral compartment joint margins. Second, images were excluded if the absolute value of the side-to-side difference in the rim measurement, i.e. the distance between the projected tibial rim and plateau measured in the medial compartment (a measure of tibial inclination), was greater than 2 mm.⁷ In addition, subjects were randomly eliminated from one site during the first year of follow-up because there were too many eligible subjects.

Statistical Analysis

The primary outcome variable for this study was the lateral joint space difference (JSD), defined as the difference between the lateral compartment joint space width in the normal knee and the ACL reconstructed knee. A positive value for the JSD indicates that the ACL reconstructed knee has a narrower joint space width than the contralateral normal knee, while a negative value for the JSD indicates that the ACL reconstructed knee has a wider joint space width than the contralateral normal knee. A paired t-test was used to test the null hypothesis that the JSD between ACL reconstructed and contralateral normal knees is similar.

Multivariable generalized linear models were constructed to assess potential predictors of JSD including age, body mass index (BMI), baseline Marx activity score, graft source, meniscus treatment, and lateral compartment chondral status. We chose these variables because they had a strong association with patient reported outcomes at 2 and 6 years in the MOON cohort from which our nested cohort was drawn.⁵ Treatment of meniscal tear was

based on the surgeon's intraoperative decision: stable tears posterior to the popliteal hiatus were not treated; unstable tears in the vascular zone were repaired; and unstable tears not amenable to repair were resected. Agreement amongst the surgeons was validated prior to the initiation of enrollment.⁶ Model assumptions of normality and heteroscedasticity were evaluated by examining Q-Q plots, estimating the optimal power parameter of a Box-Cox transformation, and performing Levene's test. All two-way were evaluated first. If not significant with a p value of 0.05 or less, the interaction terms were removed and the main effects were tested. For categorical variables with statistically significant coefficients for multiple categories, the model was run an additional time after changing the reference category for that variable to determine whether there was a statistically significant difference between the other coefficients. A p-value of 0.05 was considered statistically significant; the Holm-Bonferroni method was used to account for multiple comparisons.

Results

Subjects

At 2-year follow-up, 869 subjects were eligible for inclusion in the nested cohort, 433 patients were evaluated on-site with semi-flexed MTP radiographs, and bilateral lateral compartment JSW measurements were obtained in 358 patients. Inclusions, exclusions, and dropouts are presented in the patient flow diagram (Figure 1).

Descriptive Data

The median age of the patients was 18 years at the time of surgery. There were 170 males and 188 females. There were 196 subjects (54.7%) with the maximum Marx activity level score of 16 points. Descriptive data including meniscus treatment and articular cartilage status are presented in Table 1.

Joint Space Width

The mean lateral compartment joint space width was 7.69 mm (95% C.I.: 7.57 – 7.80 mm) for ACL reconstructed knees and 7.80 mm (95% C.I.: 7.69 – 7.91 mm) for contralateral normal knees, representing a JSD of 0.11 mm (95% C.I.: 0.03 – 0.20, $p < 0.01$). This means that on average, the ACL reconstructed knees had a narrower lateral joint space than the contralateral normal knees; 177 patients (49.4%) had a positive JSD.

In the multivariable generalized linear model, statistically significant variables that were associated with larger JSD (narrower joint space width on the ACL reconstructed side) included lateral meniscectomy ($p < 0.001$) and Marx activity level less than 16 points ($p = 0.005$; Figure 2). Lateral femoral condyle chondral defect at surgery, graft choice, age, sex and BMI were not significant (Table 2).

Two-way interactions did not reach statistical significance. Pairwise comparisons of the various meniscus treatments are shown in Table 3, but only the difference between partial lateral meniscectomy and a normal lateral meniscus was statistically significant.

Figure 3 shows radiographs of two subjects, one with joint space narrowing and one with joint space widening.

Discussion

This study of 358 patients who were injured playing a sport, were 35 or younger at the time of ACL reconstruction, and had no prior injury to either knee showed that lateral joint space width 2–3 years after surgery was 0.11 mm narrower on the ACL reconstructed side compared to the contralateral normal knee. There was more narrowing associated with partial lateral meniscectomy and in subjects with a Marx activity level less than 16 points, while there was no significant difference based on articular cartilage status, lateral meniscus repair, graft choice, age, gender, or BMI. As Figure 2 demonstrates, the average patient without partial meniscectomy did not have significant joint space narrowing while accounting for potential confounding factors.

The novel study population excluded older patients, patients with prior knee injuries, and patients who were not injured while playing a sport in order to examine the effect of injury and treatment factors on the development of post-traumatic OA. To our knowledge, this is the first prospective cohort with sufficient sample size to use multivariable regression to assess risk factors for radiographic changes in the lateral compartment after ACL reconstruction. A previous report on the medial joint space width in 262 subjects demonstrated more joint space narrowing in subjects with medial meniscus repair, partial medial meniscectomy, and increasing age.⁸ Interestingly, neither lateral meniscus repair nor age was associated with narrower lateral joint space in the current study. These findings support the notion that the medial and lateral menisci are distinct structures with differences in shape, vascularity, and mobility that may result in a varying ability to restore the joint to normal after repair.

Two previous studies measured lateral joint space width after ACL injury or ACL reconstruction and included patients with or without meniscal injury. In a cohort of 19 patients with isolated ACL tear and normal menisci treated non-operatively, there was no significant difference in lateral compartment joint space width between the ACL injured and contralateral control knee at 2–4 years post-injury.³ Although this cohort was too small to adjust for confounding factors, the findings suggest that in the absence of meniscal pathology, there was no significant lateral compartment narrowing during the first few years after ACL injury. In a matched case control study of joint space width in 39 ACL reconstructed patients with various amounts of lateral meniscal injury and 32 controls, 6 ACL reconstructed subjects at baseline had narrower lateral compartment joint space width and the overall mean lateral joint space width was 0.32 mm narrower on the ACL reconstructed knees than the contralateral knees. One additional subject had narrower lateral compartment joint space width at 4 year follow-up.¹² This cohort also had insufficient sample size to adjust for confounding factors, and there was variation in the size of lateral meniscal tear. However, this study supports our finding that lateral meniscus tear is associated with lateral compartment joint space narrowing after ACL reconstruction, although the lack of a baseline radiograph in our cohort makes us unable to determine the timing of the narrowing (before surgery versus after surgery). Furthermore, while one could argue that this absence of baseline radiographs in our cohort is a weakness, the authors of this study suggest that because of the significant abnormalities that they identified on baseline radiographs, the contralateral normal knee is a better control.

Additional studies have examined the relationship between lateral meniscal pathology and morphologic changes on radiographs obtained after surgery. A qualitative systematic review that included publications until December 2013 identified nine studies which examined the relationship between medial and lateral meniscus tears and OA.¹³ Radiographs were obtained 5–15 years after surgery and were graded by IKDC, Kellgren Lawrence or Fairbank scales. These papers presented conflicting evidence whether lateral meniscectomy was associated with OA, but the majority of studies had fewer than 100 patients and only four of nine studies accounted for confounding factors.¹³

Other studies have investigated the association between lateral meniscus pathology and MRI cartilage changes after ACL injury. In a study of 154 adults treated both operatively (n=104) and non-operatively (n=50) for ACL injury that were followed using MRI at 2 years after surgery, male sex and lateral meniscus tear were both associated with progression of cartilage defects in the lateral compartment.¹⁴ Another study of 130 subjects with MRI 2–3 years after surgery compared 62 subjects with isolated ACL tear and 38 subjects with ACL tear and either a medial or lateral meniscus tear. They showed a significant decrease in cartilage volume in the medial and patellofemoral compartments of the patients with combined injury, but no difference in the lateral compartment.¹⁵

This study is limited by the absence of baseline radiographs, which makes us unable to determine whether the lateral compartment joint space narrowing that we observed was present soon after the injury or developed gradually between the time of enrollment and follow-up at 2–3 years. While a small cohort study has shown that immediate joint space narrowing of the medial compartment does not occur after arthroscopic partial medial meniscectomy, we are not aware of any analogous study of the lateral compartment.² An additional limitation is that a lateral joint space width value could not be obtained for at least one image in 75 of 433 (17.3%) of image pairs that were analyzed, which is a product of patient positioning problems, image quality problems, and because MTP radiographs are optimized for measuring medial compartment joint space width. In addition, our nested cohort was underpowered to obtain a precise estimate of the effects of certain factors including individual grades and locations of cartilage lesions and use of allograft. Furthermore, the precise anatomical cause of the radiographic joint space changes that we observed cannot be determined from this study. The decrease in joint space could be related to a decreased volume of meniscal tissue in the joint, to a decreased volume of articular cartilage, or to meniscal extrusion.¹

Conclusions

Our novel nested cohort of 358 subjects 2–3 years after ACL reconstruction who were 35 or younger at the time of surgery, injured in sport, and had normal contralateral knees demonstrated lateral joint space narrowing on radiographs, particularly among subjects that underwent partial lateral meniscectomy and subjects with lower baseline activity levels demonstrating more narrowing. The findings from this study suggest that surgeons can tell their patients who undergo lateral meniscus repair or have a stable tear that is left in situ that they are not likely to have any increased risk of post-traumatic OA, while those that undergo arthroscopic partial meniscectomy should be advised that they have an increased risk of

developing radiographic post-traumatic OA 2–3 years after surgery. We have not been able to explain the relationship between lower activity level and narrower joint space width, so there is a possibility that this relationship is confounded by a factor that is currently unknown, and warrants further study. In addition, our methodology did not allow us to measure the progression of joint space width changes over time, so follow-up of this cohort with repeat imaging is warranted.

Acknowledgments

Research reported in this publication was partially supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Numbers K23AR066133 (M.H.J.) and R01AR053684 (K.P.S.). The content is solely the responsibility of the authors and do not necessarily represent official views of the National Institutes of Health. The project was also supported by the Vanderbilt Sports Medicine Research Fund, which received unrestricted educational gifts from Smith & Nephew Endoscopy and DonJoy Orthopaedics.

The authors acknowledge the work of radiology technologists from the Cleveland Clinic, Brendan FitzGerald RT(R), Lisa Hansinger RT(R), Jean Kovacic RT(R), Jennifer Mahony RT(R)(BD)CBDT, Katherine Malysa RT(R), Nathan Noblett RT(R), Austin Retherford RT(R), Diane Smith RT(R); from The Ohio State University Wexner Medical Center, Melissa DeSilva RT(R), Amy Hillyer RT(R), Michal Liu RT(R)(CT)(MR), Jessica Malik BSRT(R)(CT), Jennifer Pazder RT(R)(MR)(CT), Allison Phelps RT(R)(CT), Terri Sisco RT(R), James Snipes BSRT(R)(CT)(MR), Tye Thompson RT(R)(CT)(MR), Sandy Taylor RT(R)(CT); from Vanderbilt University Medical Center, Nehayet Abdulkader RT(R), Emily Cope RT(R), Danielle Dixon RT(R), Marisa Hairston-Fisher RT(R), Christopher Herod RT(R), Aleta Lovison RT(R), Julie Payne RT(R), Whitney Wise RT(R); and from Washington University and Barnes Jewish Orthopedic Center in Chesterfield, Felicia Ambus RT(R), Kathleen E Creasy RT(R), Martha Pohlman RT(R), Dianne Rehagen RT(R), Timothy Weber RT(R).

The authors also acknowledge the work of contributors invaluable for this work: for assistance with data collection from the Cleveland Clinic, Lynn Borzi MBA RN CCRC, Maxine Cox, Michelle Hines RN, Pam Koeth PA-C, Valerie Walker-Lewis, Maya McCauley, Lisa Hegemier PA-C, Leah Schmitz MPAS PA-C, Jennifer Turczyk; The Ohio State University Wexner Medical Center, Angela Pedroza MPH, Breanna Beck PA-C ATC, Isac Kunnath MS CCRC, Paul Montesanti CIP, Kari Stammen ATC; and Washington University in St. Louis, Alexandra Gada, Elizabeth Garofoli, Amanda Haas MA; for assistance with data preparation, Suzet Galindo-Martinez MS, Zhouwen Liu MS, and Charles Dupont; for assistance with statistical concerns, Frank E Harrell, Jr. PhD and Samuel Nwosu MS; for assistance with image de-identification and preparation for analysis, Baxter P Rogers PhD and Gian Franco Scaramuzza; and for data safety monitoring, Gene Hannah MD. The authors thank MOON (Multicenter Orthopaedic Outcomes Network) members from the following institutions for their support and contributions: the Hospital for Special Surgery, the Ohio State University, the University of Colorado, the University of Iowa, and Washington University in St. Louis.

We also thank all the subjects who generously enrolled and participated in this study.

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What is known about the subject

Radiographic studies using grading scales have reported predictors of post-traumatic osteoarthritis after ACL reconstruction, and one prior study has reported predictors of radiographic joint space width in the medial compartment 2–3 years after ACL reconstruction.

What this study adds to existing knowledge

This study is the first to perform multivariable analysis and report predictors of radiographic joint space width differences in the lateral compartment 2–3 years after ACL reconstruction.

Figure 1.
Flow diagram showing the selection of study participants, including all eligible and enrolled patients.

Figure 2.

Circles represent raw data points, joint space difference grouped by meniscal conditions and Marx activity level. The blue lines show the model prediction (center horizontal lines) and the 95%CI by group adjusted for age, cartilage status, gender, graft, and BMI. The horizontal dotted grey line is plotted at 0 as a visual aid. 6 data points are not shown, Marx 16 normal meniscus: -3.46, 2.31; meniscectomy: 3.1; Marx 0-15 normal meniscus: 2.19, 2.74; meniscectomy: 3.24 (all in mm).

A. Lateral Joint Space- Narrowing on the Surgical side

B. Lateral Joint Space- Widening on the Surgical side

Figure 3.

Figure 3A shows images from a patient who had a narrower lateral compartment joint space difference on the ACL reconstructed side compared to the contralateral control side. Figure 3B shows images from a patient who had a wider lateral compartment joint space difference on the ACL reconstructed side compared to the contralateral control side.

Table 1
Baseline Characteristics of Cohort

Continuous variables are shown as medians with lower and upper quartiles in parenthesis. Categorical variables are expressed as numbers with percentages in parentheses.

Age – years (IQR)	18.0 (16.0–21.8)
Sex – No. (%)	
Female	188 (52.5)
Male	170 (47.5)
Body Mass Index – kg/m ² (IQR)	23.6 (21.0–25.8)
Marx activity level – 0–16 score (IQR)	16 (12–16)
Graft Source – No. (%)	
Bone-patellar tendon-bone autograft	236 (65.9)
Hamstring autograft	103 (28.8)
Allograft	19 (5.3)
Meniscus Treatment	
No tear	163 (45.5)
Untreated tear	56 (15.6)
Repair	23 (6.4)
Partial meniscectomy	116 (32.4)
Articular Cartilage Status	
Normal/grade 1	307 (85.8)
Grade 2, 3, or 4	51 (14.2)

Key: IQR= interquartile range; No.=number; %=percentage

Table 2
Regression coefficients for the joint space difference (JSD) model

Positive values indicate the ACL reconstructed knee had narrower joint space than the contralateral control knee

Predictor	Coefficient	95% CI	P value
Intercept	0.115	−0.61 – 0.84	0.75
Age (years)	−0.013	−0.03 – 0.01	0.20
Female sex	0.09	−0.09 – 0.27	0.32
BMI (kg/m ²)	0.015	−0.01 – 0.04	0.22
Baseline Marx activity level < 16	0.28	0.08 – 0.47	0.005
Graft type			0.12
Hamstring autograft	0.20	0.01 – 0.38	NA
Allograft	0.08	−0.29 – 0.45	NA
Meniscus treatment			<0.001
Untreated tear	0.23	−0.01 – 0.47	0.06
Repair	0.18	−0.17 – 0.53	0.31
Meniscectomy	0.42	0.23 – 0.62	<0.001
Chondral lesion grade 2,3,4	0.19	−0.06 – 0.43	0.13

Table 3

Pairwise comparisons by meniscal status

Pairwise comparison	Coefficient	95% CI	P value	Adj. P value
Repair vs. meniscectomy	-0.24	-0.60 – 0.11	0.19	0.57
Untreated tear vs. meniscectomy	-0.19	-0.44 – 0.06	0.14	0.57
Meniscectomy vs. normal	0.42	0.23 – 0.62	<0.001	<0.001
Untreated tear vs. normal	0.23	-0.01 – 0.47	0.06	0.31
Repair vs. normal	0.18	-0.17 – 0.53	0.31	0.62
Untreated tear vs. repair	0.05	-0.33 – 0.43	0.81	0.81