

Predictors of Radiographic Osteoarthritis 2 to 3 Years After Anterior Cruciate Ligament Reconstruction

Data From the MOON On-site Nested Cohort

MOON Knee Group*†

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Background: Multiple studies have shown that patients are susceptible to posttraumatic osteoarthritis (PTOA) after an anterior cruciate ligament (ACL) injury, even with ACL reconstruction (ACLR). Prospective studies using multivariable analysis to identify risk factors for PTOA are lacking.

Purpose/Hypothesis: This study aimed to identify baseline predictors of radiographic PTOA after ACLR at an early time point. We hypothesized that meniscal injuries and cartilage lesions would be associated with worse radiographic PTOA using the Osteoarthritis Research Society International (OARS) atlas criteria.

Study Design: Cohort study; Level of evidence, 3.

Methods: A total of 421 patients who underwent ACLR returned on-site for standardized posteroanterior semiflexed knee radiography at a minimum of 2 years after surgery. The mean age was 19.8 years, with 51.3% female patients. At baseline, data on demographics, graft type, meniscal status/treatment, and cartilage status were collected. OARS atlas criteria were used to grade all knee radiographs. Multivariable ordinal regression models identified baseline predictors of radiographic OARS grades at follow-up.

Results: Older age (odds ratio [OR], 1.06) and higher body mass index (OR, 1.05) were statistically significantly associated with a higher OARS grade in the medial compartment. Patients who underwent meniscal repair and partial meniscectomy had statistically significantly higher OARS grades in the medial compartment (meniscal repair OR, 1.92; meniscectomy OR, 2.11) and in the lateral compartment (meniscal repair OR, 1.96; meniscectomy OR, 2.97). Graft type, cartilage lesions, sex, and Marx activity rating scale score had no significant association with the OARS grade.

Conclusion: Older patients with a higher body mass index who have an ACL tear with a concurrent meniscal tear requiring partial meniscectomy or meniscal repair should be advised of their increased risk of developing radiographic PTOA. Alternatively, patients with an ACL tear with an articular cartilage lesion can be reassured that they are not at an increased risk of developing early radiographic knee PTOA at 2 to 3 years after ACLR.

Keywords: ACL; meniscal injury; articular cartilage; knee osteoarthritis

An estimated 175,000 anterior cruciate ligament (ACL) tears occur each year in the United States,^{10,24} and ACL reconstruction (ACLR) remains the best treatment for ACL-deficient patients who desire to return to activities with pivoting or cutting requiring knee stability. Multiple studies have shown that patients are susceptible to posttraumatic osteoarthritis (PTOA) after an ACL injury, even with ACLR. A meta-analysis by Claes et al⁵ showed that

28% of patients at a minimum of 10 years after ACLR had radiographic evidence of PTOA. In a retrospective single-institution study of patients who underwent ACLR, Li et al¹³ found that medial meniscectomy, grade ≥ 2 chondrosis, longer length of follow-up, and higher body mass index (BMI) were predictors of knee osteoarthritis (OA) based on the Kellgren-Lawrence (KL) grade. Øiestad et al¹⁹ systematically reviewed the literature with a minimum 10-year follow-up and found that 0% to 13% of patients had PTOA after an isolated ACL injury and that 21% to 48% had PTOA after an ACL and concurrent meniscal injury. The authors of that study found that much of the literature

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reviewed on this topic was retrospective and had nonstandardized treatments, radiographs, and rehabilitation protocols. To establish risk factors for PTOA after an ACL injury, they concluded that future studies should be prospective, carefully evaluate all patient factors with articular cartilage and meniscal status, have sensitive outcome measures, and use multivariable regression to account for confounding variables.^{14,19}

The Multicenter Orthopaedic Outcomes Network (MOON) consortium was created in 2002 and meets the guidelines that Øiestad et al¹⁹ set for studies to evaluate the risk factors of PTOA after an ACL injury. In the current study, we report data from the MOON nested cohort, which is ideally suited to evaluate the initiation, progression, and modifiable risk factors of early PTOA after an ACL injury.²³ The MOON nested cohort consists of patients who returned on-site for a physical examination, functional testing, and radiography, including standardized posteroanterior semiflexed metatarsophalangeal (MTP) views of both knees at a minimum of 2 years after ACLR. This nested cohort includes younger patients injured during sports, with previously uninjured knees and without any preexisting risk factors for OA or prior surgical treatments. Our group previously reported data from this cohort, demonstrating that meniscectomy, meniscal repair, and age were associated with a narrower joint space 2 to 3 years after ACLR, but we also reported changes by the medial or lateral compartment.⁹ That study used a semiautomated computerized method to solely measure joint space width, whereas in the current study, we aimed to use the Osteoarthritis Research Society International (OARSI) atlas criteria, which is a whole-joint grading scale. The OARSI atlas criteria evaluate the medial and lateral compartments concurrently and assess structural changes of OA in bone (osteophytes, attrition, sclerosis) as well as in the joint space width.² Using the MOON nested cohort, we hypothesized that meniscal injuries and cartilage lesions found at the time of ACLR would be associated with worse radiographic PTOA according to OARSI grading at 2 to 3 years after ACLR.

METHODS

Participants and Data Collection

Patients were included from the MOON nested cohort who underwent ACLR between 2005 and 2010 at multiple institutions participating in the study. At the time of surgery, patients completed standardized forms with information, including demographics and the Marx activity rating

scale.¹⁶ Also at the time of surgery, surgeons filled out a standardized data collection form including graft type (bone–patellar tendon–bone autograft, hamstring tendon autograft, or allograft), medial or lateral meniscal status/treatment (no tear, untreated tear, partial meniscectomy, or meniscal repair), and medial or lateral cartilage status (modified Outerbridge classification: grade 1, normal to softening; grade 2, fissures and superficial changes; grade 3, fragmentation and deep changes; and grade 4, exposed bone). Enrolling surgeons had previously shown high reproducibility and agreement on treatments necessary for meniscal injuries and articular cartilage grading.^{7,15}

To be included in this study, patients had to be enrolled by 1 of 4 senior participating surgeons, be injured while participating in a sport, be scheduled to undergo primary ACLR without any other concomitant ligamentous surgery, have had no previous surgery on the contralateral knee, have had no subsequent revision ACLR on the index knee at the time of follow-up, and be younger than 35 years at the time of follow-up. Patients who underwent primary ACLR with a concomitant ligament injury nonoperatively treated were included. Every patient in the MOON cohort followed a standardized rehabilitation protocol.²⁶ The phases and goals included the following: phase 1 (surgery to ~2 weeks) aimed at regaining full knee range of motion and a normal gait pattern; phase 2 (~2-6 weeks) aimed at improving muscle strength and neuromuscular training; phase 3 (~7-12 weeks) aimed at running and hopping; phase 4 (~13-16 weeks) aimed at more advanced running patterns and jumping; and phase 5 (~17 weeks onward; return-to-sport phase) aimed at 85% contralateral strength, 85% contralateral on hop tests, and beginning sport-specific training. Patients returned for on-site follow-up between 2 and 3 years after primary ACLR and underwent bilateral knee radiography. The study excluded patients with image quality problems on either knee discovered upon analysis. Institutional review board approval was obtained at each of the participating institutes.

Radiographic Technique

Radiographic technologists at each participating site were trained in standardized semiflexed knee MTP views by the site's study coordinator before the study began. Consistency in positioning was ensured by using identical positioning equipment across sites. Patients were positioned with their feet in 15° of external rotation with the first MTP joint positioned directly underneath the front of the detector. Their knees were bent until the patella touched the detector. Each knee was imaged individually with the beam

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Ethical approval for this study was obtained from Vanderbilt University, the Cleveland Clinic, the University of Colorado Denver, the Hospital for Special Surgery, the University of Iowa, The Ohio State University, and Washington University in St Louis institutional review boards.

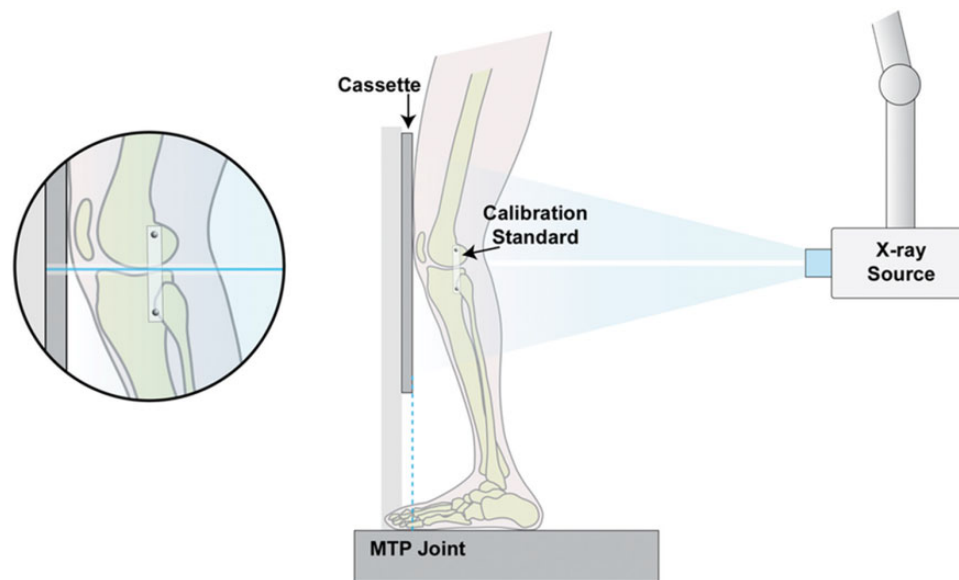


Figure 1. Schematic of the platform used to position the knee relative to the radiographic source and the cassette for the metatarsophalangeal (MTP) semiflexed knee view. Courtesy of Oksendahl et al.²⁰

directed orthogonal to the detector and focused at the center of the knee (Figure 1).

This view is similar to the described Rosenberg view,¹⁷ except that our technique provides more consistent positioning and results in a lesser degree of knee flexion, which is optimized for assessing the joint space width. Images were taken on a variety of instruments, including Polyphos (Siemens) and RADspeed (Shimadzu) machines using CR Cassettes (Agfa HealthCare) as well as Definium (GE Healthcare) and Direct Radiography (Hologic) digital machines. Semiflexed knee MTP views have shown reliability and reproducibility in multiple studies.^{4,20}

OA Classification

The OARSI atlas criteria were used to grade all knee radiographs.² The OARSI atlas criteria were used instead of the KL classification because of the KL classification's lack of sensitivity to change and the lack of distinction between the joint space and osteophyte formation.¹¹ In contrast, the OARSI atlas criteria classify knee OA from 0 to 3 based on osteophytes (medial femoral condyle, medial tibial plateau, lateral femoral condyle, and lateral tibial plateau) and for joint space narrowing (medial and lateral compartments). The system classifies medial tibial attrition, medial tibial sclerosis, and lateral femoral sclerosis as being present or absent (1 if present, 0 if absent). For the purposes of this study and analysis, a composite lateral compartment score was created from the sum of the following scores: lateral tibial plateau osteophytes, lateral femoral condyle osteophytes, lateral joint space narrowing, and lateral femoral sclerosis; the maximum possible score was 10. Similarly, a composite medial compartment score was created from the sum of the following scores: medial tibial plateau osteophytes, medial femoral condyle osteophytes, medial

joint space narrowing, medial tibial attrition, and medial tibial sclerosis, with a maximum total score of 11. A summed OARSI radiographic score has been used previously in the literature.¹ Two independent raters (an orthopaedic resident and a radiology research fellow) classified radiographs for both the surgical and nonsurgical knees. Raters were blinded to the treatment status and demographics of the patients. For radiographs with disagreement in the grading, scores were averaged.

Statistical Analysis

Interrater agreement for OARSI grading was assessed using the Cohen kappa.⁹ A linearly weighted kappa was used so that the penalty for disagreement was proportional to the distance between values made by the raters. Based on literature by Landis and Koch,¹² the following interpretation was used to judge kappa value agreement metrics: <0.00, poor; 0.00-0.20, slight; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, substantial; and 0.81-1.00, almost perfect agreement.

Multivariable ordinal regression models were used to identify statistically significant predictors of outcomes. Three outcomes included the difference in OARSI grades for the surgical knee minus the nonsurgical knee for the medial compartment, lateral compartment, and total knee (sum of the medial and lateral compartments). A positive difference indicated worse OA in the surgical knee, and a negative difference indicated less OA in the surgical knee. Baseline predictors included sex, age, BMI, Marx score, medial or lateral cartilage status, medial or lateral meniscal status/treatment, and graft type. Medial variables were excluded from models with lateral outcomes only, and lateral variables were excluded from models with medial outcomes only. Both sets of variables were included for the

combined total knee outcome. In interpreting exponentiated coefficients of the ordinal regression models, values >1 indicate a positive effect, and values <1 indicate a negative effect. All analyses were performed using the R statistical programming language (version 3.3.3; R Core Team). All testing was 2-sided, and $P < .05$ was considered statistically significant.

RESULTS

Patient Population

At minimum 2-year follow-up, 869 patients were eligible for inclusion in the nested cohort, and 433 patients returned for an on-site evaluation with bilateral knee radiographs. Of these patients, 421 were included in the analysis. Inclusions, exclusions, and dropouts are outlined in the flow diagram (Figure 2). The mean age of the analyzed cohort was 19.8 years, with 51.3% patients being female (Table 1). The lateral meniscus had a higher rate of tears (54.4%) compared with the medial meniscus (38.7%). The majority of tears of the medial meniscus were repaired, whereas most tears of the lateral meniscus required partial meniscectomy. Interrater agreement for OARSI grading of knee radiographs was within the 0.61-0.80 substantial agreement range for both compartments (Table 2).

Predictors of OA

The mean OARSI score for the lateral compartment was 2.0 ± 1.5 in the ACL-reconstructed knees versus 1.3 ± 1.1 in the contralateral normal knees. The highest lateral compartment score was 8 for the ACL-reconstructed knees and 7 for the contralateral normal knees, with a maximum possible score of 10. The mean OARSI score for the medial compartment was 2.1 ± 1.4 in the ACL-reconstructed knees versus 1.7 ± 1.1 in the contralateral normal knees. The highest medial compartment score was 8 for the ACL-reconstructed knees and 6 for the contralateral normal knees, with a maximum possible score of 11. The mean OARSI score for the total knee (composite of medial and lateral scores) was 4.1 ± 2.5 in the ACL-reconstructed knees versus 3.0 ± 1.9 in the contralateral normal knees. The highest total knee score was 13 for the ACL-reconstructed knees and 12 for the contralateral normal knees, with a maximum possible score of 21. Figure 3 displays the distributions of the 3 outcome measures, which are the differences between OARSI grades of the surgical and nonsurgical knees. Outcomes were normally distributed, with tails skewed slightly toward the right/positive values.

Using multivariable regression modeling, we found that older age (odds ratio [OR], 1.06) and higher BMI (OR, 1.05) were statistically significantly associated with a higher OARSI grade in the medial compartment compared with the contralateral knee (Table 3). Patients who underwent meniscal repair or partial meniscectomy had statistically significantly higher OARSI grades in the medial compartment (meniscal repair OR, 1.92; meniscectomy OR, 2.11) and in the lateral compartment (meniscal repair OR, 1.96;

869 Subjects Eligible

Age ≤ 35 , No concomitant ligament surgery,
No revision surgery, Injured in sport,
Surgically normal contralateral knee

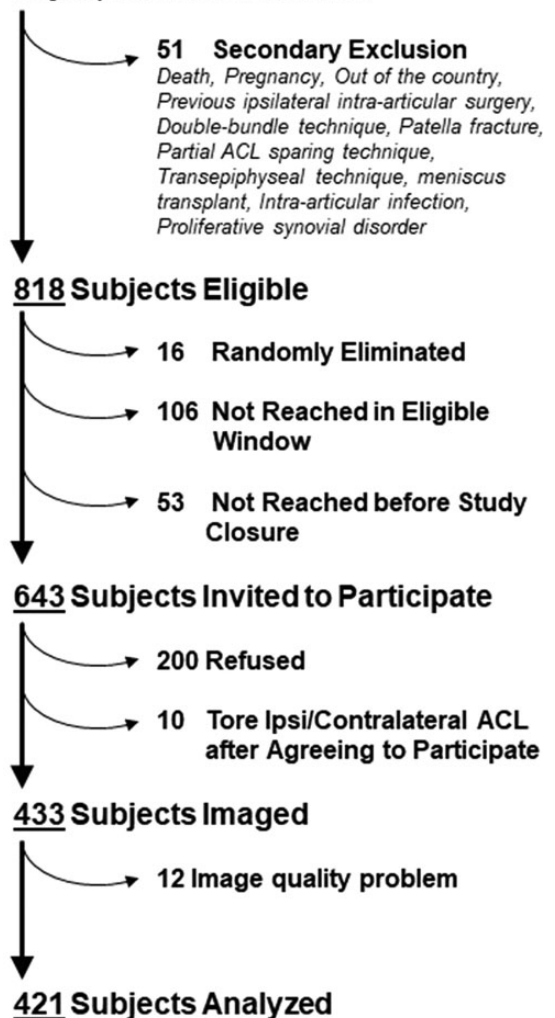


Figure 2. Patient flow diagram tabulating the total eligible patient population and the final number of patients analyzed. Sixteen patients were randomly eliminated because of resource limitations at the onset. ACL, anterior cruciate ligament; Ipsi, ipsilateral.

meniscectomy OR, 2.97) compared with the contralateral knee. Interestingly, graft type, cartilage lesions, sex, and Marx score had no significant association with any outcome.

DISCUSSION

This prospective study utilized multivariable modeling of 421 patients with knee radiographs 2 to 3 years after ACLR to predict factors leading to worse radiographic knee PTOA based on OARSI grades. We evaluated a carefully selected cohort of young patients (<35 years old at follow-up), who

TABLE 1
Baseline Patient and Surgery Characteristics^a

Sex	
Female	216 (51.3)
Male	205 (48.7)
Age, mean ± SD, y	19.8 ± 4.9
Body mass index, mean ± SD, kg/m ²	24.0 ± 3.9
Marx score, mean ± SD	13.3 ± 4.3
Medial cartilage status	
Grade 1	385 (91.4)
Grades 2-4	36 (8.6)
Medial meniscus	
No tear	258 (61.3)
Meniscal repair	85 (20.2)
Partial meniscectomy	39 (9.3)
Untreated tear	39 (9.3)
Lateral cartilage status	
Grade 1	369 (87.6)
Grades 2-4	52 (12.4)
Lateral meniscus	
No tear	192 (45.6)
Meniscal repair	30 (7.1)
Partial meniscectomy	134 (31.8)
Untreated tear	65 (15.4)
Graft	
Allograft	22 (5.2)
Bone–patellar tendon–bone autograft	255 (60.6)
Hamstring autograft	144 (34.2)

^aData are shown as n (%) unless otherwise indicated.

TABLE 2
Interrater Agreement for Radiographic OARSI Grades^a

Measure	Cohen κ (95% CI)
Medial compartment score	
Left knee	0.768 (0.671-0.866)
Right knee	0.743 (0.646-0.839)
Lateral compartment score	
Left knee	0.763 (0.662-0.863)
Right knee	0.733 (0.634-0.833)

^aOARSI, Osteoarthritis Research Society International.

were injured in sports; had undergone primary ACLR without concomitant medial collateral ligament, lateral collateral ligament, or posterior cruciate ligament surgery; had a normal contralateral knee with no history of surgery at the time of ACLR; and did not undergo subsequent ACLR to either knee at the time of follow-up. This cohort is best suited to study early PTOA after a single isolated injury event in previously normal knees. Radiographic OARSI grades were used to judge OA, and interrater agreement in this study was substantial based on the Cohen kappa.

Modeling showed that older age and higher BMI resulted in statistically significantly worse PTOA in the medial compartment of the knee. Patients who had undergone meniscal repair or partial meniscectomy had statistically significantly worse PTOA in both the medial and lateral

compartments of the knee. Partial medial and lateral meniscectomy had larger ORs (2.11 and 2.97, respectively) versus medial and lateral meniscal repair (1.92 and 1.96, respectively), suggesting that meniscectomy had a larger effect on contributing to worse PTOA in those compartments. Having an untreated meniscal tear—these are generally smaller, stable tears that are left untreated, as they are unlikely to be symptomatic—did not lead to worse PTOA in the ACL-reconstructed knee in any compartment. Interestingly, graft type, cartilage damage status, sex, and Marx score had no statistically significant positive or negative association with knee PTOA in either compartment.

Previous studies have investigated the risk factors of knee OA after ACLR. Li et al¹³ performed a retrospective cohort study of 249 patients comparing the KL grade in single-bundle ACL-reconstructed versus noninjured knees. The study used stepwise multivariable logistic regression and found that medial meniscectomy, grade ≥2 chondrosis, longer length of follow-up, and higher BMI were predictors of knee OA. Like our study, Patterson et al²¹ found that BMI and age were associated with worsening radiographic OA from 1 to 5 years after ACLR based on magnetic resonance imaging (MRI). Culvenor et al⁶ reported that, based on MRI compared with uninjured controls, meniscectomy and higher BMI predicted worse radiographic OA in patients at 1 year after ACLR. As the majority of the knee's load is borne through the medial compartment, a higher BMI could contribute to worse medial compartment PTOA.

Our group previously used a subset of this MOON nested cohort with multivariable methods to show that lateral meniscectomy and lower baseline Marx scores correlated with a narrower quantitative lateral joint space after ACLR.⁸ In a meta-analysis of 16 studies with a minimum 10 years' follow-up, Claes et al⁵ showed that after ACLR, 50% of patients undergoing meniscectomy had knee OA versus only 16% of patients not undergoing meniscectomy. Last, a systematic review of 31 studies found that the most frequent risk factor identified for knee OA development was a meniscal injury.¹⁹ Whereas many past studies have shown that meniscectomy puts a patient at risk of knee OA, the current study is novel in showing that even undergoing meniscal repair is associated with worse knee OA.

After adjusting for confounding variables, we found that both partial meniscectomy and meniscal repair were associated with worse radiographic knee PTOA even at an early time point of 2 to 3 years after ACLR. Studies have shown a 65% increase in peak joint contact stresses after only a 10% reduction in the meniscal contact area after partial meniscectomy.³ Increased stresses on the articular cartilage after partial meniscectomy could lead to accelerated OA in the injured knee. The interesting result of meniscal repair also being associated with worse radiographic knee OA based on the OARSI grade is similar to our group's past finding that medial meniscal repair was associated with a narrower quantitative joint space in the medial compartment.⁹ A separate previous study by our group revealed that lateral meniscal repair was not associated with a narrower joint space in the lateral compartment,⁸ whereas current study showed worse PTOA as defined by the OARSI grade if meniscal repair had been performed, regardless of

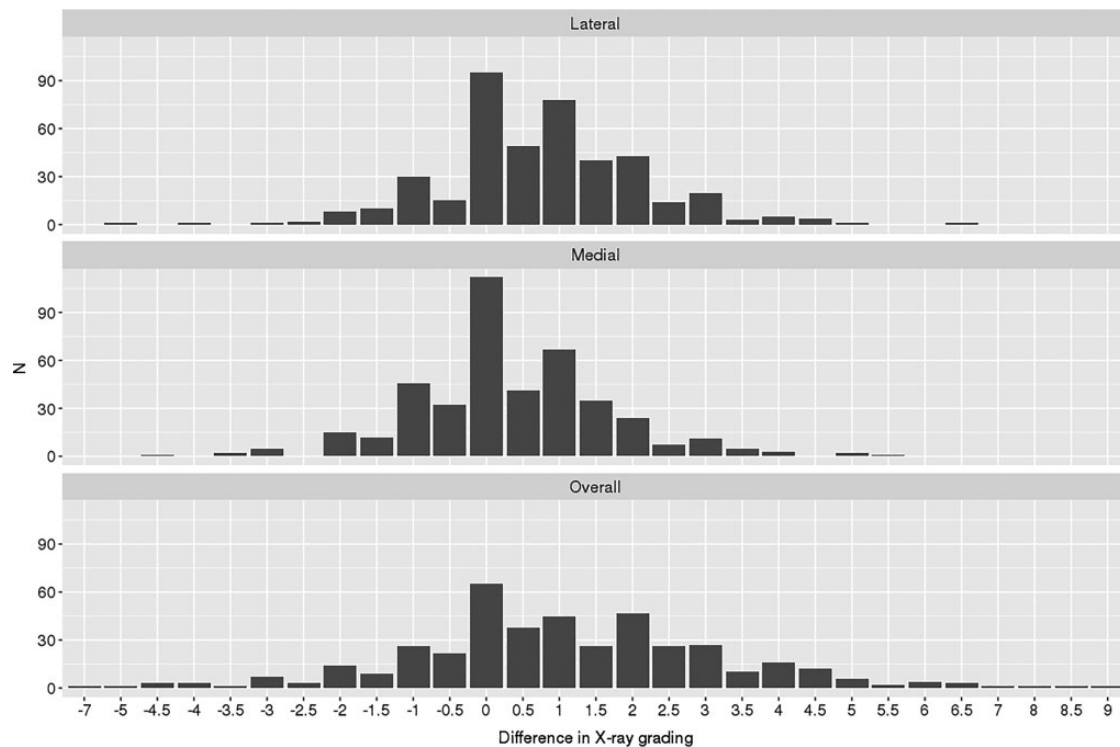


Figure 3. Histograms of the 3 outcome measures: differences between the Osteoarthritis Research Society International (OARSIS) grade of the surgical and nonsurgical knees for the lateral compartment, medial compartment, and total knee. A positive difference indicates worse posttraumatic osteoarthritis (PTOA) in the surgical knee, and a negative difference indicates less PTOA in the surgical knee; “0” indicates similar levels of PTOA in each knee.

compartment. In explaining the discrepancy, lateral meniscal repair may cause worse OARSIS grades, more driven by osteophyte formation than by lateral compartment joint space narrowing.

In a meta-analysis of meniscal repair outcomes more than 5 years postoperatively, Nepple et al¹⁸ found a 26.9% rate of meniscal repair failure (defined as reoperation or clinical failure) in ACL-reconstructed knees. It is possible that the association of worse OA in knees that have had a meniscal injury and repair could result from undiagnosed meniscal repair failure or suboptimal repaired meniscal function and the subsequent development of OA. It is also possible that larger meniscal tears requiring treatment at the time of ACLR indicate a more substantial extent of knee injury, either at the time of initial ACL failure or during subsequent instability episodes. The more rapid onset of OA may reflect a dose-response effect to an injury rather than an isolated treatment effect.

Remarkably, articular cartilage lesions, one of our hypothesized predictors of worse radiographic knee OA, did not affect the outcomes of the medial or lateral compartment OARSIS grade. This study grouped cartilage damage from grades 2 to 4 together because of patient number limitations, so seeing the effect of only severe grade 4 cartilage damage was not feasible. It is possible that the time frame of the current study was too short to see the effect of articular cartilage lesions, although a similar finding was shown in a work by Shelbourne et al²² that assessed the outcomes

of articular cartilage injuries at a mean of 8.7 years after an ACL injury. The authors found no difference in radiographic International Knee Documentation Committee scores between patients with and without chondral injuries. Focal articular cartilage damage after an ACL injury may not lead to more widespread whole compartment radiographic OA. An additional longer term follow-up study is needed to definitively answer this important clinical question.

One limitation of this study is that no baseline radiographs were available for grading, so the OARSIS grade of the injured knee was compared with that of the contralateral knee to determine the amount of PTOA in the ACL-reconstructed knee. Without baseline radiographs, this method is unable to assess the longitudinal change in OA in the injured knee. However, it could be argued that comparing the injured knee with the contralateral healthy knee could serve as a better control. The use of the contralateral nonsurgical knee as a control to evaluate early PTOA in ACLR is also supported in a study by Tourville et al²⁵ and other similar studies.^{8,13} Compared with the injured knee, the healthy uninjured knee would have the same stressors of activity level, genetics, biology, age, and all other unmeasured factors within the patient. Interestingly, there was a subset of patients in whom the OARSIS grade was better in the injured knee. This could be because of radiography-based grading not being precise in borderline patients, which makes having a large sample size

TABLE 3
Regression Modeling for Difference in OARSI Grades^a

Predictor	Lateral Compartment		Medial Compartment		Total Knee	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Sex						
Female	—	—	—	—	—	—
Male	1.29 (0.89-1.87)	.182	1.23 (0.86-1.76)	.259	1.26 (0.87-1.83)	.221
Age	0.98 (0.94-1.02)	.293	1.06 (1.02-1.10)	.006	1.02 (0.98-1.06)	.435
BMI	1.02 (0.97-1.07)	.488	1.05 (1.00-1.10)	.048	1.04 (0.99-1.09)	.111
Marx score	0.99 (0.95-1.04)	.742	1.02 (0.98-1.07)	.377	1.01 (0.96-1.05)	.787
Graft		.637 ^b		.887 ^b		.820 ^b
BPTB autograft	—	—	—	—	—	—
Hamstring autograft	1.15 (0.79-1.66)	.458	0.93 (0.64-1.35)	.717	1.08 (0.74-1.58)	.678
Allograft	1.33 (0.61-2.90)	.476	1.11 (0.51-2.41)	.791	1.25 (0.56-2.80)	.589
Lateral cartilage status						
Grade 1	—	—	—	—	—	—
Grades 2-4	0.85 (0.50-1.45)	.559			1.47 (0.85-2.55)	.171
Lateral meniscus		<.001 ^b				.002^b
No tear	—	—	—	—	—	—
Meniscal repair	1.96 (1.00-3.83)	.049			1.32 (0.66-2.66)	.430
Partial meniscectomy	2.97 (1.95-4.54)	<.001			2.21 (1.46-3.34)	<.001
Untreated tear	1.10 (0.68-1.79)	.690			1.05 (0.64-1.72)	.844
Medial cartilage status						
Grade 1			—	—	—	—
Grades 2-4			1.56 (0.81-2.98)	.181	1.01 (0.52-1.96)	.985
Medial meniscus				.006^b		.020^b
No tear			—	—	—	—
Meniscal repair			1.92 (1.23-3.01)	.004	1.83 (1.17-2.87)	.008
Partial meniscectomy			2.11 (1.13-3.93)	.019	1.72 (0.91-3.24)	.094
Untreated tear			0.91 (0.50-1.68)	.773	0.85 (0.47-1.53)	.582

^aOR values >1 indicate a positive effect or worse posttraumatic osteoarthritis in the anterior cruciate ligament-reconstructed knee, and OR values <1 indicate a negative effect; “1” indicates similar odds in both knees. Bold indicates that the value is statistically significant ($P < .05$). BMI, body mass index; BPTB, bone-patellar tendon-bone; OARSI, Osteoarthritis Research Society International; OR, odds ratio.

^bP values from a likelihood ratio test are shown for factors with >2 levels.

and using multivariable modeling very important to adjust for this.

In addition, this study did not investigate preoperative knee mechanical alignment, as varus or valgus alignment might predispose to medial or lateral changes, longitudinal BMI data, or laxity data and the effect that residual laxity/instability might have on joint wear. Other limitations are that a short-term assessment at 2 to 3 years may fail to detect changes that will occur over a longer time frame and that the OARSI atlas criteria may not be sensitive enough to detect the earliest changes of PTOA.

CONCLUSION

Multivariable analysis of our unique cohort of 421 patients who returned for follow-up knee radiography a minimum of 2 years after ACLR showed that older age and higher BMI were associated with worse radiographic PTOA in the medial compartment and that meniscal repair and partial meniscectomy were both associated with worse radiographic PTOA in the medial and lateral compartments. This study shows that radiographic OA can occur at an early time point (2-3 years) in some patients after an ACL

injury. These results are best used in patient counseling about the risks of OA after injuries and surgery. Older patients with a higher BMI who have an ACL tear with a concurrent meniscal tear requiring partial meniscectomy or meniscal repair should be advised of their increased risk of developing radiographic OA. Alternatively, patients with an ACL tear with an articular cartilage lesion or with a meniscal tear not requiring treatment can be reassured that they are not at an increased risk of developing early knee OA within 2 to 3 years after ACLR.

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REFERENCES

1. Akelman MR, Fadale PD, Hulstyn MJ, et al. Effect of matching or over-constraining knee laxity during ACL reconstruction on knee osteoarthritis and clinical outcomes: a randomized controlled trial with 84 month follow up. *Am J Sports Med.* 2016;44(7):1660-1670.
2. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cartilage.* 2007;15:A1-A56.
3. Brindle T, Nyland J, Johnson DL. The meniscus: review of basic principles with application to surgery and rehabilitation. *J Athl Train.* 2001;36(2):160-169.
4. Buckland-Wright JC, Ward RJ, Peterfy C, Mojcik CF, Leff RL. Reproducibility of the semiflexed (metatarsophalangeal) radiographic knee position and automated measurements of medial tibiofemoral joint space width in a multicenter clinical trial of knee osteoarthritis. *J Rheumatol.* 2004;31(8):1588-1597.
5. Claes S, Hermie L, Verdonk R, Bellemans J, Verdonk P. Is osteoarthritis an inevitable consequence of anterior cruciate ligament reconstruction? A meta-analysis. *Knee Surg Sports Traumatol Arthrosc.* 2013;21(9):1967-1976.
6. Culvenor AG, Collins NJ, Guermazi A, et al. Early knee osteoarthritis is evident one year following anterior cruciate ligament reconstruction: a magnetic resonance imaging evaluation. *Arthritis Rheumatol.* 2015;67(4):946-955.
7. Dunn WR, Wolf BR, Amendola A, et al. Multirater agreement of arthroscopic meniscal lesions. *Am J Sports Med.* 2004;32(8):1937-1940.

8. Jones MH, Moon Knee Group, Spindler KP, et al. Differences in the lateral compartment joint space width after anterior cruciate ligament reconstruction: data from the MOON onsite cohort. *Am J Sports Med.* 2018;46(4):876-882.
9. Jones MH, Spindler KP, Fleming BC, et al. Meniscus treatment and age associated with narrower radiographic joint space width 2-3 years after ACL reconstruction: data from the MOON onsite cohort. *Osteoarthritis Cartilage.* 2015;23(4):581-588.
10. Kaeding CC, Léger-St-Jean B, Magnussen RA. Epidemiology and diagnosis of anterior cruciate ligament injuries. *Clin Sports Med.* 2017;36(1):1-8.
11. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. *Clin Orthop.* 2016;474(8):1886-1893.
12. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977;33(1):159-174.
13. Li RT, Lorenz S, Xu Y, Harner CD, Fu FH, Irrgang JJ. Predictors of radiographic knee osteoarthritis after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2011;39(12):2595-2603.
14. Magnussen RA, Mansour AA, Carey JL, Spindler KP. Meniscus status at anterior cruciate ligament reconstruction associated with radiographic signs of osteoarthritis at 5- to 10-year follow-up: a systematic review. *J Knee Surg.* 2009;22(4):347-357.
15. Marx RG, Connor J, Lyman S, et al. Multirater agreement of arthroscopic grading of knee articular cartilage. *Am J Sports Med.* 2005;33(11):1654-1657.
16. Marx RG, Stump TJ, Jones EC, Wickiewicz TL, Warren RF. Development and evaluation of an activity rating scale for disorders of the knee. *Am J Sports Med.* 2001;29(2):213-218.
17. Melnic CM, Gordon JL, Courtney PM, Sheth NP. A systematic approach to evaluating knee radiographs with a focus on osteoarthritis. *Journal of Orthopedics and Rheumatology.* 2014;2(1):6.
18. Nepple JJ, Dunn WR, Wright RW. Meniscal repair outcomes at greater than five years. *J Bone Joint Surg Am.* 2012;94(24):2222-2227.
19. Øiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury. *Am J Sports Med.* 2009;37(7):1434-1443.
20. Oksendahl HL, Gomez N, Thomas CS, et al. Digital radiographic assessment of tibiofemoral joint space width: a variance component analysis. *J Knee Surg.* 2009;22(3):205-212.
21. Patterson BE, Culvenor AG, Barton CJ, et al. Worsening knee osteoarthritis features on magnetic resonance imaging 1 to 5 years after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2018;46(12):2873-2883.
22. Shelbourne KD, Jari S, Gray T. Outcome of untreated traumatic articular cartilage defects of the knee: a natural history study. *J Bone Joint Surg Am.* 2003;85(suppl 2):8-16.
23. Spindler KP, Parker RD, Andrich JT, et al. Prognosis and predictors of ACL reconstructions using the MOON cohort: a model for comparative effectiveness studies. *J Orthop Res.* 2013;31(1):2-9.
24. Spindler KP, Wright RW. Anterior cruciate ligament (ACL) tear. *N Engl J Med.* 2008;359(20):2135-2142.
25. Tourville TW, Johnson RJ, Slauterbeck JR, Naud S, Beynon BD. Assessment of early tibiofemoral joint space width changes after anterior cruciate ligament injury and reconstruction: a matched case-control study. *Am J Sports Med.* 2013;41(4):769-778.
26. Wright RW, Haas AK, Anderson J, et al. Anterior cruciate ligament reconstruction rehabilitation. *Sports Health.* 2015;7(3):239-243.