



Published in final edited form as:

*J Orthop Res.* 2017 July ; 35(7): 1366–1374. doi:10.1002/jor.23557.

## Risk factors for Radiographic Joint Space Narrowing and Patient Reported Outcomes of Post-Traumatic Osteoarthritis after ACL Reconstruction: Data from the MOON Cohort

**Morgan H. Jones, M.D.** and

Cleveland Clinic Foundation, Orthopaedic Surgery, Cleveland, Ohio U.S.A

**Kurt P. Spindler, M.D.**

Cleveland Clinic Foundation, Orthopaedic Surgery, Cleveland, Ohio U.S.A

### Abstract

The Multicenter Orthopaedic Outcomes Network (MOON) is an NIH-funded prospective, longitudinal cohort of over 3500 patients who have undergone anterior cruciate ligament reconstruction (ACLR) by 14 sports medicine surgeons at 7 academic medical centers. Patient reported outcome questionnaires (PRO's) are completed at baseline and multiple timepoints after surgery, and a nested cohort of patients return for radiographs to assess the development of joint space changes. We review the risk factors for worse patient reported outcomes, the predictors of clinically significant symptoms of post-traumatic osteoarthritis (PTOA), and the factors associated with more radiographic joint space narrowing. Baseline PRO's were highly predictive of follow-up scores. Factors associated with worse PRO's at 2 and 6 years included female sex, higher BMI, smoking, less education, allograft, medial meniscectomy or repair, and chondral injury. Partial lateral meniscectomy was unexpectedly associated with better PRO's. Factors associated with clinically significant symptoms of PTOA at 2 and 6 years included subsequent surgery, meniscal pathology, and chondral injury. Factors associated with narrower medial compartment joint space width included medial meniscectomy, medial meniscus repair, and increased age. Medial joint space width was slightly wider overall for the ACLR knees compared to the contralateral normal knees. Future studies will evaluate PRO's and radiographs at 10 year follow-up.

### Introduction/Body

Approximately 130,000 ACL reconstructions are performed in the United States each year<sup>1</sup>, and the operation is successful at restoring functional knee stability and enabling patients to return to athletic activities. However, the ACL-injured knee is at significant risk of developing post-traumatic osteoarthritis even after ACL reconstruction.<sup>2–5</sup> Systematic reviews have shown that over 50 percent of patients will have radiographic signs of osteoarthritis 10–20 years after ACL reconstruction, and this risk is increased in patients who have concomitant meniscus tears.<sup>6</sup> Because many people who sustain ACL tears are

---

Corresponding author: spindlk@ccf.org.

Author Contributions:

Morgan H. Jones: Conception and design of the project, drafting of the manuscript

Kurt P Spindler: Conception and design of the project, critical revision of the manuscript

young athletes, they are faced with the development of symptomatic post-traumatic osteoarthritis in their third and fourth decades, and this represents a significant public health problem that affects thousands of people in their prime working years.

The multicenter orthopaedic outcomes network (MOON) is a NIH funded and IRB approved prospective longitudinal multicenter cohort study that was designed to follow ACL reconstruction patients after surgery to determine their clinical outcomes including risk factors for the initiation and progression of osteoarthritis. The subjects were enrolled from the practices of 14 fellowship trained sports medicine surgeons at 7 academic medical centers beginning in 2002. Subjects completed an enrollment form that captured demographic factors including age, gender, race / ethnicity; social history factors including smoking status, education level, occupation, and sports participation; characteristics of the injury including the sport or activity at the time of injury; and validated patient reported outcomes including the SF-36, KOOS, IKDC, and Marx activity level questionnaires. Surgeons also completed a data form at the time of surgery that documented physical examination findings, intraoperative findings including meniscus and articular cartilage status, and details of treatment including graft choice, fixation, meniscus treatment, and articular cartilage treatment. Subjects were followed up at 2 and 6 years with the same questionnaire that they completed at baseline.<sup>7-11</sup>

A novel nested cohort within MOON was established to evaluate the initiation and progression of OA in young active patients without previous knee injury.<sup>12</sup> To be eligible for entry into this nested cohort, subjects had to be 35 or younger at 2 year follow up, injured while doing a sport, have no previous knee injury and no graft rupture during the follow up period, and have no history of surgery on the contralateral knee. These subjects were brought back to their enrollment site to have a physical examination by a surgeon blinded to their treatment status and side of surgery, KT-1000 measurement and hop testing by a physical therapist blinded to treatment status, and standardized radiographs to assess radiographic joint space width.

Over 3500 patients have been enrolled in MOON since the inception of the study in 2002. The nested cohort includes 425 patients enrolled from 2005–2012. The MOON investigators have published over 40 manuscripts from the cohort including baseline associations between clinical findings and symptoms<sup>13</sup>, success of meniscus repair<sup>14,15</sup>, predictors of activity level<sup>16</sup>, predictors of graft failure<sup>17,18</sup>, and cost effectiveness of ACL reconstruction<sup>19,20</sup>. The focus of this article will be the findings from MOON that evaluate the risk factors for developing symptomatic and radiographic OA including patient reported outcomes at 2 and 6 years in the full cohort, significant knee pain at 2 and 6 years in the full cohort, and radiographic joint space measurement in the nested cohort.

## **Risk factors for worse patient reported outcomes 6 years after ACL reconstruction**

For large cohort studies such as MOON that seek to follow large groups of patients from several sites at multiple time points, validated patient reported outcome measures allow assessment of patient symptoms that may be associated with osteoarthritis. MOON

evaluated 1512 ACL patients who entered the cohort from 2002–2004 and completed 2 and 6 year follow-up. Follow-up was obtained in 87 percent of patients at 2 years and 86 percent of patients at 6 years; there were 56 percent males with a median age of 23 years at the time of surgery. Models were constructed for the IKDC, the 5 KOOS subscales, and the Marx activity level scale, and the scores were treated as continuous variables. Follow up time (2 versus 6 years) was also included as a predictor in each of the models.<sup>9</sup> Data are presented in tables 1–7.

For the IKDC outcome, the following demographic characteristics were significantly associated with worse outcome: female sex, higher BMI, smoking, and lower education level. Patients with lower baseline Marx activity level scores had worse outcomes, and those who had reconstruction with allograft had worse outcomes than those with autograft. Meniscus pathology predicted outcome, but some of the findings were surprising. Patients with medial meniscus repair or partial medial meniscectomy had worse outcome than those with a normal or untreated meniscus tear. Interestingly, those with a normal lateral meniscus actually had worse outcomes than those with a partial lateral meniscectomy. As expected, the presence of articular cartilage injury at baseline predicted worse outcomes at follow-up: patients with grade 3 or 4 articular cartilage changes of the medial femoral condyle, lateral femoral condyle, or medial tibial plateau had worse outcomes than those without these changes. Patients with worse baseline IKDC had worse IKDC at 2 and 6 year follow up. Odds ratios and confidence intervals are listed in table 1.

For the KOOS outcomes, the same demographic characteristics except for female sex had a significant association with worse outcome for all subscales. Medial meniscus repair, but not partial medial meniscectomy, was associated with a worse outcome for all subscales. Interestingly, normal lateral meniscus had worse outcomes than untreated tear for all subscales, and worse outcomes than partial meniscectomy for 2/5 subscales. Grade 3 or 4 articular cartilage lesions of the medial femoral condyle, lateral femoral condyle, medial tibial plateau, lateral tibial plateau, and trochlea predicted worse outcomes on some but not all subscales. Similar to the IKDC outcomes, allograft predicted worse outcomes than autograft; in addition, hamstring autograft predicted worse KOOS sports and recreation function while patellar tendon autograft predicted worse KOOS symptoms. Baseline Marx score was not associated with worse outcome for any KOOS subscale. Similar to the IKDC outcome, patients with worse baseline scores had worse KOOS scores at follow up. Odds ratios and confidence intervals for each KOOS outcome are listed in tables 2–7.

In summary, meniscus and articular cartilage pathology were significant predictors of both IKDC and KOOS patient reported outcomes at 2 and 6 years after ACL reconstruction in the MOON cohort. While articular cartilage pathology, medial meniscus repair, and partial medial meniscectomy predicted worse outcomes, partial lateral meniscectomy and untreated lateral meniscus tear were unexpectedly associated with better outcomes. This finding was unexpected because one would assume that injury to the meniscus would result in increased contact stress in the affected compartment and subsequent more rapid development of osteoarthritis. One possible rationale for our counterintuitive finding may be that the ACL injury episode is associated with a dissipation of force through the knee joint, and when the force is absorbed by the lateral meniscus (resulting in a tear), the joint fares better over the

long term than if the force is absorbed by other tissues such as the articular cartilage surfaces. The finding that baseline PRO scores were a strong predictor of follow up scores at both 2 and 6 years post-operatively was particularly interesting because this may represent a modifiable risk factor; recent studies of preoperative rehabilitation prior to ACL reconstruction have suggested that rehabilitation interventions that improve baseline PRO scores may result in improved post-operative outcomes.<sup>21</sup>

## Symptoms of post-traumatic osteoarthritis – KOOS thresholds for painful or symptomatic knee

While the evaluation of continuous outcomes such as the KOOS subscales and IKDC can be useful for assessing the risk factors of pain, function, and symptoms after ACL reconstruction, it can sometimes be difficult to assess the factors that are most associated with clinically significant symptoms of post-traumatic OA. In an effort to address this problem, data from the MOON cohort was modeled to determine the predictors of symptomatic knee OA as defined by three different methods.<sup>22</sup>

The first method was based on Englund et al. who described patients with sufficient knee symptoms to seek medical care according to their KOOS scores.<sup>23</sup> They defined the symptomatic knee as KOOS knee-related quality of life  $\leq 87.5$ , and two or more other subscales below the following values: KOOS pain  $\leq 86.1$ , KOOS symptoms  $\leq 85.7$ , KOOS activities of daily living  $\leq 86.8$ , and KOOS sports and recreation  $\leq 85.0$ . The second method defined the symptomatic knee as a KOOS pain subscore greater than 2 standard deviations below the mean value for athletic populations with a history of knee ligament injury. This reported mean value was  $92.3 \pm 10$  points, which made the cutoff value 72.3 points, which also corresponded to the OARSI responder criteria for effective interventions in OA of 20 points on the KOOS pain subscale.<sup>24</sup> Models were constructed to evaluate predictors of a symptomatic knee at both 2 and 6 years using the first two methods. The third method was designed to identify patients with progression of knee symptoms from the 2 year to the 6 year follow-up, defined by a decrease in the KOOS pain subscale of 10 points or more, which corresponds to the minimal clinically important difference for the subscale in athletic populations. The analysis included 1761 patients with follow up 2 and 6 years after ACL reconstruction. The median age was 23 years. There was 87 percent follow up at 2 years and 86 percent follow up at 6 years.<sup>22</sup>

The only consistent statistically significant risk factor for predicting a painful knee by the first two methods at both 2 and 6 years was subsequent surgery on the same knee, which occurred in 22 percent of patients at 6 years (324/1506). Subsequent surgeries included revision ACL (113 cases); hardware removal, manipulation, or other arthroscopic surgery (205 cases); and total knee replacement (6 cases). The odds ratio of subsequent surgery for predicting a symptomatic knee was greater than 2 for all models (range 2.20 – 3.41,  $p < 0.001$  for all models). Higher baseline BMI predicted a symptomatic knee at 2 years but not 6 years for both of the first two methods. Lower Marx activity level at baseline did not predict a symptomatic knee at either 2 or 6 years, but lower Marx activity level at 2 years predicted a symptomatic knee at 6 years for both of the first two methods. Interestingly, none of the

surgical factors (articular cartilage lesions, meniscus treatment, or graft choice) that had predicted worse knee scores with modeling of continuous outcomes was a consistent predictor of a symptomatic knee at 2 or 6 years with either of the first two methods.<sup>22</sup>

The third method determined knees that had significant worsening of KOOS pain from 2 to 6 years. Significant predictors of worsening included subsequent surgery ( $p=0.06$ ), female gender ( $p=0.03$ ), previous meniscal pathology prior to the ACL reconstruction ( $p=0.04$ ), grade 3 or 4 medial tibial plateau chondral lesions ( $p=0.02$ ), and grade 3 or 4 patella chondral lesions ( $p=0.03$ ).<sup>22</sup>

In summary, modeling the predictors of a symptomatic knee at 2 and 6 years after ACL reconstruction provides an opportunity to identify patients who may be developing the symptoms of osteoarthritis and to determine the risk factors for developing these symptoms. The most consistent and strongest predictor of a symptomatic knee at 2 and 6 years post-operatively in multivariable modeling was subsequent surgery, which in some cases may be associated with the severity of the initial injury, but in many cases may be related to a modifiable risk factor such as graft choice.

## **Signs of post-traumatic osteoarthritis – medial tibiofemoral joint space width**

A nested cohort was established within the overall MOON cohort to assess the initiation and progression of post-traumatic OA in younger patients injured during athletic activity without prior knee problems. This group of patients had standardized bilateral posteroanterior metatarsophalangeal joint radiographs to assess joint space width.<sup>25</sup> The feet were positioned in 15 degrees external rotation and the knees were bent until the patellae touched the detector. Knees were imaged individually, and a standard was used to allow calibration for differences in magnification. Technicians were trained at each site and used identical positioning equipment. The radiographs were measured using a semi-automated computerized method that delineates the femoral and tibial joint margins and quantifies the minimum joint space width in the medial compartment.<sup>26</sup> Because patients were excluded from the cohort if they had a contralateral knee ligament injury or knee surgery, comparisons of joint space width were made between the ACL reconstructed side and contralateral normal knee.<sup>12</sup>

Joint space width measurements were obtained for 262 patients who had ACL reconstruction surgery between 2005–2010 and were recruited into the nested cohort. The average age at the time of surgery was 20 years (range 12–33). The mean medial compartment minimum joint space width was 5.06 mm (95% CI 4.96–5.15 mm) in the ACL reconstructed knees compared to 4.71 mm (95% CI 4.62–4.80 mm) in the contralateral normal knees, which was significantly wider for the ACL reconstructed knees ( $p<0.001$ ). In fact, 194 subjects (74%) had a wider joint space width on the ACL reconstructed side. This finding was unexpected, as we had hypothesized that early post-traumatic osteoarthritis in the ACL reconstructed knees would have resulted in narrowing more often than widening of the medial joint space.<sup>12</sup> However, this is consistent with magnetic resonance images from the Knee ACL non-operative versus operative treatment (KANON) study that showed an increase in

cartilage volume of the central portion of the medial femoral condyle in 61 subjects who had ACL injury followed by early reconstruction, delayed reconstruction, or physical therapy.<sup>27</sup>

In addition, a multivariable model was constructed to predict the difference in medial compartment minimum joint space width between the ACL reconstructed and contralateral normal knees. The model included the following variables that were selected based on their strong associations with patient reported outcomes in the overall cohort: age, BMI, baseline Marx activity level, graft source, medial meniscus treatment, and medial femoral condyle articular cartilage status. Variables that predicted a narrower joint space in the ACL reconstructed knee compared to the contralateral normal knee included increased age ( $p < 0.001$ ), meniscus repair ( $p = 0.001$ ), and meniscectomy ( $p < 0.001$ ). The difference in minimum joint space width was greater for meniscectomy (0.64 mm, 95% CI 0.38–0.90mm) than for meniscus repair (0.31 mm, 95% CI 0.12–0.49mm), and the difference per year of age was 0.042 mm (95% CI 0.025–0.058mm).<sup>12</sup>

This imaging study may have been more sensitive to change if MRI images would have been available both pre- and post-operatively for evaluation of the articular cartilage, as MRI has been very successful at detecting the early manifestations of post-traumatic osteoarthritis after ACL injury.<sup>{27–30}</sup> For example, similar findings regarding meniscus treatment were demonstrated in a much smaller study of 62 patients that underwent MRI with T2 relaxation time evaluation after ACL reconstruction. Articular cartilage T2 values were significantly higher for the meniscal repair and partial meniscectomy knees compared to the knees with normal menisci, with no significant difference between the meniscectomy and repair groups.<sup>31</sup> However, we feel that standardized posteroanterior radiographs with a semiautomated joint space width measurement technique can provide an excellent cost effective alternative to post-operative MRI that could be incorporated into clinical practice, and radiographic joint space width measurement has actually been as sensitive as MRI for detecting progression of osteoarthritis in some cohorts.<sup>32</sup>

In summary, medial meniscus treatment and age are significant predictors of medial compartment joint space narrowing 2–3 years after ACL reconstruction in young, active patients without prior knee injury. The wider medial compartment joint space width was unexpected; this may represent the early manifestation of post-traumatic OA, or possibly an adaptive change of cartilage biology that may prevent the progression of post-traumatic OA. This analysis also demonstrates the first time that radiographic changes have been detected at such an early time-point in a prospective cohort with uniform post-operative rehabilitation and sufficient numbers to perform multivariable modeling.

## Conclusion

The MOON project has provided substantial insight into the initiation and development of post-traumatic OA after ACL reconstruction in a multicenter population cohort study. Multivariable modeling of patient reported outcomes has identified meniscus and articular cartilage status as significant predictors of outcome at 2 and 6 years post-operatively. When the data were analyzed to predict the presence of a symptomatic knee, the strongest predictor was subsequent surgery. Finally, analysis of joint space width in a nested cohort of younger

patients with previously uninjured knees showed that medial meniscus repair, partial meniscectomy, and increasing age all were associated with more joint space narrowing 2–3 years post-operatively.

While the study could have gleaned more information from the cohort by obtaining additional data such as pre- and post-operative MRI, synovial fluid or serum biomarkers, or PRO's from additional time points, the cohort still remains the largest prospective multicenter cohort of ACL reconstructions to publish results with over 85 percent follow-up at 2 and 6 years.

Future studies in MOON will evaluate patient reported outcomes and the presence of a symptomatic knee at 10 year follow up and additional follow up will also allow repeat analysis with a substantially larger sample size. Future analysis of radiographs will be performed to assess predictors of lateral joint space width, and re-imaging of the subcohort with standardized MTP radiographs will be repeated at 10 year follow-up.

## Acknowledgments

Research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Numbers R01 AR053684 and K23AR066133. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

We would also like to thank: the MOON team members and Elizabeth Sosic, project manager

## References

1. Mall NA, Chalmers PN, Moric M, et al. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *The American journal of sports medicine*. 2014; 42(10):2363–2370. [PubMed: 25086064]
2. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *The American journal of sports medicine*. 2007; 35(10):1756–1769. [PubMed: 17761605]
3. Ichiba A, Kishimoto I. Effects of articular cartilage and meniscus injuries at the time of surgery on osteoarthritic changes after anterior cruciate ligament reconstruction in patients under 40 years old. *Arch Orthop Trauma Surg*. 2009; 129(3):409–415. [PubMed: 19050905]
4. Li RT, Lorenz S, Xu Y, et al. Predictors of radiographic knee osteoarthritis after anterior cruciate ligament reconstruction. *The American journal of sports medicine*. 2011; 39(12):2595–2603. [PubMed: 22021585]
5. Lohmander LS, Ostenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum*. 2004; 50(10):3145–3152. [PubMed: 15476248]
6. Oiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. *The American journal of sports medicine*. 2009; 37(7):1434–1443. [PubMed: 19567666]
7. Dunn WR, Spindler KP, MOON Consortium. Predictors of activity level 2 years after anterior cruciate ligament reconstruction (ACLR): a Multicenter Orthopaedic Outcomes Network (MOON) ACLR cohort study. 2010:11.
8. Dunn WR, Spindler KP, Amendola A, et al. Which preoperative factors, including bone bruise, are associated with knee pain/symptoms at index anterior cruciate ligament reconstruction (ACLR)? A Multicenter Orthopaedic Outcomes Network (MOON) ACLR Cohort Study. *The American journal of sports medicine*. 2010; 38(9):1778–1787. [PubMed: 20595556]

9. Cox CL, Huston LJ, Dunn WR, et al. Are Articular Cartilage Lesions and Meniscus Tears Predictive of IKDC, KOOS, and Marx Activity Level Outcomes After Anterior Cruciate Ligament Reconstruction?: A 6-Year Multicenter Cohort Study. *The American journal of sports medicine*. 2014
10. Spindler KP, Parker RD, Andrish 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. [PubMed: 22912340]
11. Spindler KP, Huston LJ, Wright RW, et al. The prognosis and predictors of sports function and activity at minimum 6 years after anterior cruciate ligament reconstruction: a population cohort study. *The American journal of sports medicine*. 2011; 39(2):348–359. [PubMed: 21084660]
12. 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. *Osteoarthr Cartil*. 2015
13. Dunn WR, Spindler KP, Amendola A, et al. Which preoperative factors, including bone bruise, are associated with knee pain/symptoms at index anterior cruciate ligament reconstruction (ACLR)? A Multicenter Orthopaedic Outcomes Network (MOON) ACLR Cohort Study. 2010:10.
14. Westermann RW, Wright RW, Spindler KP, et al. Meniscal repair with concurrent anterior cruciate ligament reconstruction: operative success and patient outcomes at 6-year follow-up. *The American journal of sports medicine*. 2014; 42(9):2184–2192. [PubMed: 25023440]
15. Toman CV, Dunn WR, Spindler KP, et al. Success of meniscal repair at anterior cruciate ligament reconstruction. *The American journal of sports medicine*. 2009; 37(6):1111–1115. [PubMed: 19465734]
16. Dunn WR, Spindler KP. MOON Consortium. Predictors of activity level 2 years after anterior cruciate ligament reconstruction (ACLR): a Multicenter Orthopaedic Outcomes Network (MOON) ACLR cohort study. *The American journal of sports medicine*. 2010; 38(10):2040–2050. [PubMed: 20709944]
17. Borchers JR, Pedroza A, Kaeding C. Activity level and graft type as risk factors for anterior cruciate ligament graft failure: a case-control study. *The American journal of sports medicine*. 2009; 37(12):2362–2367. [PubMed: 19684294]
18. Kaeding CC, Aros B, Pedroza A, et al. Allograft Versus Autograft Anterior Cruciate Ligament Reconstruction: Predictors of Failure From a MOON Prospective Longitudinal Cohort. *Sports Health*. 2011; 3(1):73–81. [PubMed: 23015994]
19. Mather RC, Hettrich CM, Dunn WR, et al. Cost-Effectiveness Analysis of Early Reconstruction Versus Rehabilitation and Delayed Reconstruction for Anterior Cruciate Ligament Tears. *The American journal of sports medicine*. 2014; 42(7):1583–1591. [PubMed: 24801663]
20. Mather RC. Societal and Economic Impact of Anterior Cruciate Ligament Tears. *J Bone Joint Surg Am*. 2013; 95(19):1751–9. [PubMed: 24088967]
21. Failla MJ, Logerstedt DS, Grindem H, et al. Does Extended Preoperative Rehabilitation Influence Outcomes 2 Years After ACL Reconstruction? A Comparative Effectiveness Study Between the MOON and Delaware-Oslo ACL Cohorts. *The American journal of sports medicine*. 2016; 44(10):2608–2614. [PubMed: 27416993]
22. Wasserstein D, Huston LJ, Nwosu S, et al. KOOS pain as a marker for significant knee pain two and six years after primary ACL reconstruction: a Multicenter Orthopaedic Outcomes Network (MOON) prospective longitudinal cohort study. *Osteoarthr Cartil*. 2015; 23(10):1674–1684. [PubMed: 26072385]
23. Englund M, Roos EM, Lohmander LS. Impact of type of meniscal tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. *Arthritis Rheum*. 2003; 48(8):2178–2187. [PubMed: 12905471]
24. Dougados M, Leclaire P, van der Heijde D, et al. esponse criteria for clinical trials on osteoarthritis of the knee and hip: a report of the Osteoarthritis Research Society International Standing Committee for Clinical Trials response criteria initiative. 2000:395–403.
25. 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. [PubMed: 19634723]



26. Duryea J, Li J, Peterfy CG, et al. Trainable rule-based algorithm for the measurement of joint space width in digital radiographic images of the knee. *Med Phys*. 2000; 27(3):580–591. [PubMed: 10757609]
27. Frobell RB. Change in cartilage thickness, posttraumatic bone marrow lesions, and joint fluid volumes after acute ACL disruption: a two-year prospective MRI study of sixty-one subjects. *The Journal of Bone and Joint Surgery*. 2011; 93(12):1096–1103. [PubMed: 21776546]
28. Eckstein F, Wirth W, Lohmander LS, et al. Five-year followup of knee joint cartilage thickness changes after acute rupture of the anterior cruciate ligament. *Arthritis & Rheumatology*. 2015; 67(1):152–161. [PubMed: 25252019]
29. Frobell RB, Le Graverand M-P, Buck R, et al. The acutely ACL injured knee assessed by MRI: changes in joint fluid, bone marrow lesions, and cartilage during the first year. *Osteoarthritis Cartilage*. 2009; 17(2):161–167. [PubMed: 18760637]
30. Amano K, Pedoia V, Su F, et al. Persistent Biomechanical Alterations After ACL Reconstruction Are Associated With Early Cartilage Matrix Changes Detected by Quantitative MR. *Orthopaedic Journal of Sports Medicine*. 2016; 4(4):1–10.
31. Li H, Chen S, Tao H. Quantitative MRI T2 Relaxation Time Evaluation of Knee Cartilage: Comparison of Meniscus-Intact and -Injured Knees After Anterior Cruciate Ligament Reconstruction. *The American journal of sports medicine*. 2015 0363546514564151.
32. Wirth W, Duryea J, Hellio Le Graverand M-P, et al. Direct comparison of fixed flexion, radiography and MRI in knee osteoarthritis: responsiveness data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2013; 21(1):117–125. [PubMed: 23128183]

**Table 1**

Significant predictors and confidence interval outcomes for IKDC scores 6 years after ACL reconstruction

Predictor	(Comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		2.27	(1.80–2.87)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.32	(1.04–1.67)	2 years
Age		N.S.		
Gender	(male vs. female)	0.72	(0.58–0.88)	Females
BMI	(23 vs. 28)	0.79	(0.69–0.91)	Higher BMI
Smoking status	(never vs. quit)	0.61	(0.44–0.83)	Quit smoking
	(never vs. current)	0.49	(0.36–0.67)	Current smoker
Education	(12 vs. 16 years)	1.35	(1.11–1.64)	Less education
Baseline Marx		1.32	(1.00–1.75)	Lower Marx
Reconstruction type	(primary vs. revision)	0.40	(0.28–0.57)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	0.64	(0.48–0.85)	yes
Medial meniscus repair	(no tear vs. repair)	0.68	(0.52–0.89)	Repair
Medial meniscectomy	(no tear vs. 17% excised)	0.64	(0.46–0.90)	Excision
	(no tear vs. 33% excised)	0.73	(0.54–0.99)	Excision
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	1.38	(1.07–1.77)	No tear
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	1.84	(1.07 – 3.15)	No tear
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	0.45	(0.26–0.80)	Grade 4
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	0.60	(0.39–0.92)	Grade 3
	(nl/grade 1 vs. grade 4)	0.40	(0.21–0.74)	Grade 4
MTP cartilage	(grade 2 vs. grade 3/4)	N.S.		
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for IKDC scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 2**

Significant predictors and confidence interval outcomes for KOOS symptom scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		2.11	(1.67–2.66)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.63	(1.28–2.07)	2 years
Age		N.S.		
Gender	(male vs. female)	N.S.		
BMI	(23 vs. 28)	0.88	(0.78–1.00)	Higher BMI
Smoking status	(never vs. quit)	0.65	(0.47–0.91)	Quit smoking
	(never vs. current)	0.58	(0.42–0.79)	Current smoker
Education	(12 vs. 16 years)	1.48	(1.21–1.81)	Less education
Baseline Marx		N.S.		
Reconstruction type	(primary vs. revision)	0.55	(0.40–0.77)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	N.S.		
Medial meniscus repair	(no tear vs. repair)	0.62	(0.47–0.83)	repair
Medial meniscectomy	(no tear vs. 17% excised)	0.57	(0.38–0.86)	excision
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	1.55	(1.21–1.99)	No tear
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	1.95	(1.13–3.38)	No tear
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	N.S.		
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	0.64	(0.42–1.00)	Grade 3
	(nl/grade 1 vs. grade 4)	0.51	(0.28–0.97)	Grade 4
MTP cartilage	(grade 2 vs. grade 3/4)	0.30	(0.12–0.80)	Grade 3/4
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for KOOS symptom scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 3**

Significant predictors and confidence interval outcomes for KOOS pain scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		2.28	(1.81–2.87)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.63	(1.26–2.11)	2 years
Age		N.S.		
Gender	(male vs. female)	N.S.		
BMI	(23 vs. 28)	0.84	(0.73–0.95)	Higher BMI
Smoking status	(never vs. quit)	0.58	(0.42–0.80)	Quit smoking
	(never vs. current)	0.58	(0.41–0.83)	Current smoker
Education	(12 vs. 16 years)	1.39	(1.14–1.70)	Less education
Baseline Marx		N.S.		
Reconstruction type	(primary vs. revision)	0.49	(0.36–0.68)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	N.S.		
Medial meniscus repair	(no tear vs. repair)	0.68	(0.52–0.88)	repair
Medial meniscectomy	(no tear vs. 17% excised)	N.S.		
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	2.11	(1.23–3.64)	No tear
Lateral meniscus	(no tear vs. no treatment)	1.64	(1.29–2.09)	No tear
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	N.S.		
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	0.46	(0.25–0.83)	Grade 4
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	N.S.		
	(nl/grade 1 vs. grade 4)	N.S.		
MTP cartilage	(grade 2 vs. grade 3/4)	0.39	(0.17–0.90)	Grade 3/4
LTP cartilage	(nl/grade 1 vs. grade 2)	1.47	(1.05–2.08)	nl/grade 1
	(grade 2 vs. grade 3/4)	0.48	(0.25–0.95)	Grade 3/4
Trochlea	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for KOOS pain scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 4**

Significant predictors and confidence interval outcomes for KOOS ADL scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		2.61	(2.09–3.26)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.66	(1.26–2.19)	2 years
Age		N.S.		
Gender	(male vs. female)	N.S.		
BMI	(23 vs. 28)	0.79	(0.69–0.91)	Higher BMI
Smoking status	(never vs. quit)	0.57	(0.42–0.77)	Quit smoking
	(never vs. current)	0.51	(0.37–0.70)	Current smoker
Education	(12 vs. 16 years)	1.57	(1.27–1.93)	Less education
Baseline Marx		N.S.		
Reconstruction type	(primary vs. revision)	0.50	(0.35–0.72)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	0.70	(0.51–0.95)	Yes
Medial meniscus repair	(no tear vs. repair)	0.71	(0.53–0.94)	repair
Medial meniscectomy	(no tear vs. 17% excised)	N.S.		
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	1.55	(1.20–2.01)	No tear
Lateral meniscus repair	(no tear vs. repair)	1.56	(1.07–2.28)	No tear
Lateral meniscectomy	(no tear vs. 50% excised)	2.18	(1.21–3.93)	No tear
	(no tear vs. 67% excised)	1.70	(1.00–2.87)	No tear
MFC cartilage	(nl/grade 1 vs. grade 4)	N.S.		
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	N.S.		
	(nl/grade 1 vs. grade 4)	N.S.		
MTP cartilage	(grade 2 vs. grade 3/4)	N.S.		
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea	(nl/grade 1 vs. grade 3/4)	0.49	(0.28–0.85)	Grade 3/4

Significant predictors of outcome for KOOS ADL scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 5**

Significant predictors and confidence interval outcomes for KOOS Sports/Recreation scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		2.13	(1.67–2.70)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.50	(1.17–1.91)	2 years
Age		N.S.		
Gender	(male vs. female)	N.S.		
BMI	(23 vs. 28)	0.82	(0.72–0.93)	Higher BMI
Smoking status	(never vs. quit)	N.S.		
	(never vs. current)	0.58	(0.41–0.81)	Current smoker
Education	(12 vs. 16 years)	1.42	(1.16–1.74)	Less education
Baseline Marx		N.S.		
Reconstruction type	(primary vs. revision)	0.49	(0.34–0.70)	Revision
Graft source	(BTB vs. hamstring)	1.28	(1.02–1.60)	Hamstring
Prior ACL other knee	(yes vs. no)	0.72	(0.53–0.98)	Yes
Medial meniscus repair	(no tear vs. repair)	0.65	(0.50–0.84)	repair
Medial meniscectomy	(no tear vs. 17% excised)	N.S.		
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	1.60	(1.26–2.03)	No tear
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	N.S.		
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	N.S.		
	(nl/grade 1 vs. grade 2)	1.36	(1.02–1.82)	nl/grade 1
LFC cartilage	(nl/grade 1 vs. grade 3)	N.S.		
	(nl/grade 1 vs. grade 4)	N.S.		
MTP cartilage	(grade 2 vs. grade 3/4)	N.S.		
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for KOOS Sports/Recreation scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 6**

Significant predictors and confidence interval outcomes for KOOS Quality of Life scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		1.58	(1.27–1.98)	Lower baseline
Follow up time	(2 years vs. 6 years)	1.47	(1.15–1.86)	2 years
Age		N.S.		
Gender	(male vs. female)	N.S.		
BMI	(23 vs. 28)	0.86	(0.75–0.98)	Higher BMI
Smoking status	(never vs. quit)	0.69	(0.50–0.93)	Quit smoking
	(never vs. current)	0.63	(0.45–0.87)	Current smoker
Education	(12 vs. 16 years)	1.30	(1.06–1.59)	Less education
Baseline Marx		N.S.		
Reconstruction type	(primary vs. revision)	0.39	(0.27–0.56)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	0.71	(0.53–0.95)	Yes
Medial meniscus repair	(no tear vs. repair)	0.63	(0.49–0.83)	repair
Medial meniscectomy	(no tear vs. 17% excised)	N.S.		
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	1.41	(1.10–1.81)	No tear
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	N.S.		
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	0.40	(0.23–0.71)	Grade 4
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	N.S.		
	(nl/grade 1 vs. grade 4)	0.42	(0.20–0.89)	Grade 4
MTP cartilage	(grade 2 vs. grade 3/4)	0.39	(0.19–0.78)	Grade 3/4
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea cartilage	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for KOOS Quality of Life scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)

**Table 7**

Significant predictors and confidence interval outcomes for Marx Activity Level scores 6 years after ACL reconstruction

Predictor	(comparison)	Coefficient	(95% CI)	Worse Outcome
Baseline score		3.33	(2.51–4.42)	Lower baseline
Follow up time	(2 years vs. 6 years)	0.45	(0.35–0.58)	6 years
Age	(15 vs. 35 years)	0.38	(0.24–0.62)	Older age
Gender	(male vs. female)	0.52	(0.42–0.62)	Females
BMI	(23 vs. 28)	0.83	(0.73–0.95)	Higher BMI
Smoking status	(never vs. quit)	N.S.		
	(never vs. current)	0.66	(0.50–0.89)	Current smoker
Education	(12 vs. 16 years)	1.22	(1.02–1.45)	Less education
Reconstruction type	(primary vs. revision)	0.56	(0.40–0.78)	Revision
Graft source	(BTB vs. hamstring)	N.S.		
Prior ACL other knee	(yes vs. no)	N.S.		
Medial meniscus repair	(no tear vs. repair)	N.S.		
Medial meniscectomy	(no tear vs. 17% excised)	N.S.		
	(no tear vs. 33% excised)	N.S.		
	(no tear vs. 50% excised)	N.S.		
Lateral meniscus	(no tear vs. no treatment)	N.S.		
Lateral meniscus repair	(no tear vs. repair)	N.S.		
Lateral meniscectomy	(no tear vs. 50% excised)	N.S.		
	(no tear vs. 67% excised)	N.S.		
MFC cartilage	(nl/grade 1 vs. grade 4)	0.47	(0.24–0.92)	Grade 4
	(nl/grade 1 vs. grade 2)	N.S.		
LFC cartilage	(nl/grade 1 vs. grade 3)	N.S.		
	(nl/grade 1 vs. grade 4)	N.S.		
MTP cartilage	(grade 2 vs. grade 3/4)	N.S.		
LTP cartilage	(nl/grade 1 vs. grade 2)	N.S.		
	(grade 2 vs. grade 3/4)	N.S.		
Trochlea cartilage	(nl/grade 1 vs. grade 3/4)	N.S.		

Significant predictors of outcome for Marx Activity Level scores 6 years after ACL reconstruction ( $p < 0.05$ ). (MFC – medial femoral condyle, LFC – lateral femoral condyle, MTP – medial tibial plateau, LTP – lateral tibial plateau, nl – normal, N.S. – not significant)