Published in final edited form as:

Am J Sports Med. 2016 January ; 44(1): 143–151. doi:10.1177/0363546515608475.

Decreased Knee Joint Loading Associated With Early Knee Osteoarthritis After Anterior Cruciate Ligament Injury

Elizabeth Wellsandt, PT^{†,*}, Emily S. Gardinier, PhD[‡], Kurt Manal, PhD[†], Michael J. Axe, MD^{†,§}, Thomas S. Buchanan, PhD[†], and Lynn Snyder-Mackler, PT, ScD[†]

[†]University of Delaware, Newark, Delaware, USA.

[‡]University of Michigan, Ann Arbor, Michigan, USA.

[§]First State Orthopaedics, Newark, Delaware, USA.

Abstract

Background—Anterior cruciate ligament (ACL) injury predisposes individuals to early-onset knee joint osteoarthritis (OA). Abnormal joint loading is apparent after ACL injury and reconstruction. The relationship between altered joint biomechanics and the development of knee OA is unknown.

Hypothesis—Altered knee joint kinetics and medial compartment contact forces initially after injury and reconstruction are associated with radiographic knee OA 5 years after reconstruction.

Study Design—Case-control study; Level of evidence, 3.

Methods—Individuals with acute, unilateral ACL injury completed gait analysis before (baseline) and after (posttraining) preoperative rehabilitation and at 6 months, 1 year, and 2 years after reconstruction. Surface electromyographic and knee biomechanical data served as inputs to an electromyographically driven musculoskeletal model to estimate knee joint contact forces. Patients completed radiographic testing 5 years after reconstruction. Differences in knee joint kinetics and contact forces were compared between patients with and those without radiographic knee OA.

Results—Patients with OA walked with greater frontal plane interlimb differences than those without OA (nonOA) at baseline (peak knee adduction moment difference: 0.00 ± 0.08 N·m/kg·m [nonOA] vs -0.15 ± 0.09 N·m/kg·m [OA], $P = .014$; peak knee adduction moment impulse difference: -0.001 ± 0.032 N·m·s/kg·m [nonOA] vs -0.048 ± 0.031 N·m·s/kg·m [OA], $P = .042$). The involved limb knee adduction moment impulse of the group with osteoarthritis was also lower than that of the group without osteoarthritis at baseline (0.087 ± 0.023 N·m·s/kg·m [nonOA] vs 0.049 ± 0.018 N·m·s/kg·m [OA], $P = .023$). Significant group differences were absent at posttraining but reemerged 6 months after reconstruction (peak knee adduction moment difference: 0.02 ± 0.04 N·m/kg·m [nonOA] vs -0.06 ± 0.11 N·m/kg·m [OA], $P = .043$). In

For reprints and permission queries, please visit SAGE's Web site at <http://www.sagepub.com/journalsPermissions.nav>

*Address correspondence to Elizabeth Wellsandt, PT, University of Delaware, 540 South College Avenue, Suite 210Z, Newark, DE 19713, USA (ewellsan@udel.edu).

Investigation performed at the University of Delaware Newark Delaware USA

One or more of the authors has declared the following potential conflict of interest

addition, the OA group walked with lower peak medial compartment contact forces of the involved limb than did the group without OA at 6 months (2.89 ± 0.52 body weight [nonOA] vs 2.10 ± 0.69 body weight [OA], $P = .036$).

Conclusion—Patients who had radiographic knee OA 5 years after ACL reconstruction walked with lower knee adduction moments and medial compartment joint contact forces than did those patients without OA early after injury and reconstruction.

Keywords

contact force; knee moment; loading; osteoarthritis; anterior cruciate ligament

The risk of knee osteoarthritis (OA) dramatically increases after anterior cruciate ligament (ACL) reconstruction (ACLR).^{3,13,29} Patients with ACL injury experience higher rates of knee OA at much younger ages compared with noninjured individuals.⁴⁰ The hallmark osteoarthritic symptom of pain may be absent at the onset of knee OA,^{23,41} while the presence of chronic knee pain in younger individuals is not well associated with radiographic OA.^{18,40} Patient-reported outcomes of knee function are also poor discriminators for the presence of knee OA after ACL injury and ACLR.^{23,41} Thus, the initial development and progression of OA after ACL injury can be difficult to predict and detect without the use of routine imaging. Evidence of altered biomechanics has been demonstrated early after ACL injury and ACLR,^{44,57} and abnormal joint loading is a key mechanism that may contribute to the early development of OA. Identifying a link between joint loading and OA is a critical step in better understanding and possibly preventing early-onset knee joint OA.

Common surrogate measures of knee joint loading are frontal and sagittal plane knee moments. Higher external knee moments have been associated with the presence and severity of idiopathic knee OA in older populations.^{12,32,33,37} However, external knee adduction and flexion moments have been reported to be lower in the limb at risk for OA after ACLR.^{50,54,57} Although it is clear that knee kinetics are altered after ACL injury and ACLR, there is a lack of information about the effect of abnormal biomechanics on the later development of OA.

The external knee adduction moment is widely used as an indicator of knee joint loading of the medial tibiofemoral compartment.^{10,12,32,33,37,58} The knee adduction moment before ACLR has not been well characterized, while values higher than, equal to, and lower than the contralateral knee and healthy controls have been reported at varying points in time after ACLR.^{5,39,48,51–53, 57} Conflicting reports of the knee adduction moment after surgery may be due to longitudinal changes in frontal plane kinetics after ACLR.⁵²

Patients initially walk with decreased external knee flexion moments after ACL injury.^{16,28,43,44,54} However, it is unclear how long these alterations persist after ACLR.^{24,42,52,53} As with the knee adduction moment, it is not well understood whether unresolved alterations in the knee flexion moment after ACL injury and ACLR are detrimental to long-term knee joint health.

Knee joint contact forces estimated by use of musculoskeletal models are another method to quantify knee joint loading. Models incorporating electromyographic (EMG) data may provide a more comprehensive understanding of the knee's loading environment after ACL injury than do joint moments alone, because these models can incorporate the contribution of muscular co-contraction in the estimation of joint contact forces.^{4,56} Patients walk with asymmetric knee joint contact forces after ACL injury,¹⁵ and some demonstrate persistent asymmetries 6 months after ACLR.¹⁴ However, it is unknown whether these abnormal loading patterns precede early-onset knee OA.

The purpose of this study was to determine whether knee joint moments and contact forces early after injury and ACLR were associated with radiographic knee OA 5 years after surgery. Drawing from previous work that demonstrated lower knee joint kinetics,^{16,28,43,44,54,57} muscle forces,¹⁶ and joint contact forces¹⁵ after ACL injury, we hypothesized that altered knee frontal and sagittal plane kinetics and medial compartment contact forces initially after injury and ACLR would be associated with medial compartment knee OA 5 years after ACLR.

METHODS

Subjects

Twenty-two subjects between the ages of 14 and 51 years with complete, unilateral ACL injury within the previous 7 months were included in this study as part of a larger randomized controlled trial of 55 patients.²⁰ All patients were regular participants in International Knee Documentation Committee activity level I or II cutting and pivoting activities^{7,21} before injury and demonstrated dynamic knee instability after injury (noncopers).¹¹ Exclusion criteria included concomitant repairable meniscus injuries, grade III injury to other knee ligaments, and full-thickness articular cartilage lesion larger than 1 cm² diagnosed before ACLR or contralateral ACL injury after initial ACLR.

Patients were enrolled in this study after effusion, range of motion (ROM), pain, and obvious gait impairments were resolved by use of the physical therapy protocol described by Hurd et al.²⁶ Study approval was granted by the institutional review board at the University of Delaware, and all patients provided written informed consent. After study enrollment, patients received additional preoperative rehabilitation to further restore lower extremity strength and neuromuscular control.²⁰ All patients underwent ACLR by a single, board-certified orthopaedic surgeon using either a 4-bundle semitendinosus-gracilis autograft or soft tissue allograft with a medial and lateral portal and medial parapatellar tendon incision. No surgical procedures were performed on any additional ligamentous knee structures. Patients completed progressive, criterion-based postoperative rehabilitation early after surgery.¹

Testing

Testing consisted of gait analysis with EMG at 5 time points: (1) preoperatively after rehabilitation to resolve effusion, ROM, pain, and obvious gait impairments (baseline); (2) immediately after 10 sessions of additional preoperative rehabilitation (posttraining); (3) 6

months after ACLR after criterion-based rehabilitation (6 months); (4) 1 year after ACLR; and (5) 2 years after ACLR.

Gait analysis was completed by use of an 8-camera system (VICON; Oxford Metrics Ltd) sampled at 120 Hz and 1 force platform (Bertec Corp) sampled at 1080 Hz. Retroreflective markers were placed on bony landmarks at each lower extremity, with rigid shells containing markers placed at the pelvis, thighs, and shanks.¹⁶ Patients walked at self-selected speed, which was maintained ($\pm 5\%$) throughout the testing session and subsequent testing sessions. Stance phase joint angles and moments were calculated by use of inverse dynamics within commercial software (Visual 3D; C-Motion). Moments were normalized to mass (kilograms) and height (meters). Variables of interest included the peak external knee adduction moment, external knee adduction moment impulse during stance phase, and peak external knee flexion moment. Differences between limbs were calculated for each kinetic measure (involved minus uninvolved).

Surface EMG was collected at 1080 Hz (MA-300 EMG System; Motion Lab Systems) for 7 muscles on each limb (rectus femoris, medial and lateral vasti, semitendinosus, long head of biceps femoris, and medial and lateral gastrocnemii). Patients completed maximal voluntary isometric contractions for each muscle group to normalize EMG amplitude during subsequent walking trials. Raw EMG data were high-pass filtered (second-order Butterworth, 30 Hz), rectified, and then low-pass filtered (second-order Butterworth, 6 Hz), creating a linear envelope for maximal voluntary isometric contractions and walking trials.

EMG-Driven Modeling

Gait analysis and surface EMG data served as inputs to a musculoskeletal model^{16,36} for the estimation of joint contact forces. This model has demonstrated good repeatability¹⁵ and high accuracy when validated by use of in vivo contact force data recorded from an instrumented knee prosthesis.³⁶ In addition, sensitivity analyses conducted on varying experimental inputs to the model have demonstrated that interlimb differences in peak contact forces found within this study are much larger than estimated potential error.¹⁵ Contact forces for 10 of these patients were included in the primary analyses of knee joint contact forces after acute ACL injury (“baseline” time point [Gardinier et al¹⁶]) and after ACLR (“6 months” time point [Gardinier et al¹⁶]).

The EMG-driven model of the knee included an anatomic model that characterizes the musculoskeletal geometry,⁸ an activation dynamics model that characterizes the transformation of EMG (the neural signal) to muscle activation, and a contraction dynamics model that contains a Hill-type muscle model and characterizes the transformation of muscle activation to muscle force. The anatomic model contained pelvis, femur, tibia, and foot segments that were actuated by 10 muscle-tendon units and scaled according to subject anthropometry. The activation dynamics and contraction dynamics models contained adjustable muscle parameters (see Gardinier et al¹⁶) that are difficult to accurately measure in vivo, including optimal muscle fiber length and tendon slack length. These parameters were adjusted during a subject-specific model calibration and were allowed to vary within physiological bounds as described previously (see Gardinier et al¹⁶ for limits used). After

the model was calibrated, muscle forces were predicted for the stance phase of 3 novel overground walking trials.

Medial compartment contact force was calculated by balancing the external knee adduction moment (expressed about the lateral compartment contact point, which was fixed at a distance of 25% of tibial plateau width from the knee joint center) with the internal adduction moments due to the muscle forces and the contact force in the medial compartment.⁵⁶ The peak medial compartment contact force occurring in the first half of stance was the discrete variable of interest for this study, and the average of 3 trials was used for analysis.

Radiographs

Weightbearing posteroanterior (PA) bent knee (30°) radiographs were completed 5 years after ACLR and graded by use of the Kellgren-Lawrence (KL) system.³⁰ The presence of OA was defined as a KL grade 2 in the medial compartment (graded by E.W.; between-day kappa statistic: 0.904, $P < .001$; all KL grades verified by a board-certified orthopaedic surgeon). Initial radiographs after ACL injury were not obtained; however, articular cartilage lesions were assessed during arthroscopic evaluation at the time of ACLR. Two patients demonstrated chronic articular cartilage changes at the medial femoral condyle during arthroscopic evaluation during ACLR. One of these 2 patients had OA in the medial compartment at 5 years, and the other did not.

Statistical Analysis

Statistical analyses were completed with PASSW 23.0 software (SPSS Inc). Independent t tests and Fisher exact tests were performed to test differences in demographics, baseline characteristics, and concomitant injuries between patients without radiographic knee OA (nonOA group) and those with OA (OA group) in the medial compartment 5 years after ACLR. Independent t tests were used to test differences in loading measures for the involved limb between the nonOA and OA groups (peak knee adduction moment, knee adduction moment impulse, peak knee flexion moment, and peak medial compartment contact force) and interlimb differences between groups at each time point for each of these measures. Effect sizes were calculated for group differences in loading measures.⁶ Previously reported minimally detectable changes were used to determine meaningful asymmetry between limbs for peak knee adduction moment (0.06 N·m/kg·m), peak knee flexion moment (0.09 N·m/kg·m), and peak medial compartment contact force (0.30 body weight [BW]).¹⁷ Statistical significance was set at $P = .05$.

RESULTS

In total, 22 subjects returned for radiographic testing 5 years after ACLR (15 nonOA, 7 OA) (Figure 1). Of these 22 subjects, the number completing testing at each of the 5 earlier time points is described in Table 1. A greater proportion of subjects who completed testing at 2 years who had OA at 5 years were female (nonOA: 9 males, 2 females; OA: 1 male, 4 females; $P = .036$). No further group differences existed for sex at other time points (Table 1). No differences in age, mass, body mass index (BMI), preinjury activity level, time from

injury to baseline, time from injury to ACLR, or graft type were present between groups (Table 1). The OA group walked more slowly than the nonOA group at 1 year (nonOA: 1.64 ± 0.12 m/s, OA: 1.49 ± 0.04 m/s; $P = .035$) but not at any other testing sessions (Table 1). The presence of concomitant meniscal or articular cartilage injuries identified arthroscopically during ACLR did not differ between groups at any time point for all compartments of the involved knee or specifically the medial tibiofemoral compartment (Table 1). No differences existed in additional knee injuries or surgeries sustained between the time of initial ACL injury and 5-year radiographic testing (nonOA: 1 ipsilateral retear, 1 ipsilateral partial posterior cruciate ligament tear and meniscus tear; OA: 1 ipsilateral retear) (Table 1).

The OA group walked with lower peak knee adduction moment than the nonOA group, with significant interlimb differences and large effect sizes present at baseline (peak knee adduction moment difference: 0.00 ± 0.08 N·m/kg·m [nonOA] vs -0.15 ± 0.09 N·m/kg·m [OA]; $P = .014$) (Figure 2, A and B; see also the Appendix, available online at <http://ajsm.sagepub.com/supplemental>). Asymmetric peak frontal plane moments improved in the OA group after preoperative rehabilitation, but significant group differences were again present at 6 months after ACLR (peak knee adduction moment difference: 0.02 ± 0.04 N·m/kg·m [nonOA] vs -0.06 ± 0.11 N·m/kg·m [OA]; $P = .043$) (Figure 2B). Both groups demonstrated symmetry in peak knee adduction moment at 1 and 2 years after surgery (Figure 2B). Large group differences for the involved limb peak knee adduction moment were present at baseline but no further time points (Figure 2A).

Additional frontal plane group differences were present in the knee adduction moment impulse (online Appendix). At baseline, the OA group had lower knee adduction moment impulse at the involved limb than did the nonOA group (0.087 ± 0.023 N·m·s/kg·m [nonOA] vs 0.049 ± 0.018 N·m·s/kg·m [OA]; $P = .023$) (Figure 2C) and unloaded the involved limb compared with the contralateral limb (knee adduction moment impulse difference: -0.001 ± 0.032 N·m·s/kg·m [nonOA] vs -0.048 ± 0.031 N·m·s/kg·m [OA]; $P = .042$) with large effect sizes exhibited (Figure 2D). Group differences in knee adduction moment impulse were absent after preoperative rehabilitation and continued through 1 year after surgery. At 2 years, no differences at the involved limbs existed between groups in the knee adduction moment impulse, but the OA group had a significantly lower interlimb difference (lower knee adduction moment impulse on the involved limb, represented by a negative knee adduction moment impulse difference) than the nonOA group (knee adduction moment impulse difference: 0.010 ± 0.018 N·m·s/kg·m [nonOA] vs -0.021 ± 0.032 N·m·s/kg·m [OA]; $P = .027$) (Figure 2, C and D).

There were large differences between limbs in peak knee flexion moment for both the OA and nonOA groups at baseline, with both groups demonstrating lower sagittal plane moments on their involved knee (Figure 2, E and F, online Appendix). Large interlimb differences continued in the OA group at 6 months. However, these differences did not reach statistical significance between groups at either time point.

Large group differences in peak medial compartment contact forces of involved limbs were seen at baseline, 6 months, and 1 year, reaching statistical significance at 6 months (peak

medial compartment contact force: 2.89 ± 0.52 BW [nonOA] vs 2.10 ± 0.69 BW [OA]; $P = .036$) (Figure 2G and online Appendix). Large interlimb differences were also present between groups at baseline and 6 months (Figure 2H). Neither involved limb peak medial compartment contact force nor interlimb differences in peak medial compartment contact force were different between groups after preoperative rehabilitation.

DISCUSSION

The purpose of this study was to determine whether loading measures before and after ACLR were associated with knee OA 5 years after surgery. Results indicate that compared with subjects without radiographic OA 5 years after surgery, those who did develop radiographic OA walked with lower moments and contact forces at the involved limb and had greater interlimb differences early after injury and ACLR. Differences were largest and statistically significant before preoperative rehabilitation and 6 months after ACLR.

The current findings are consistent with a growing body of evidence suggesting that joint unloading, not overloading, may be associated with the cascade of early degenerative changes at the knee after ACL injury.^{2,57} Koo and Andriacchi³¹ suggested that healthy cartilage increases in thickness in response to higher repetitive loading during walking, whereas Koo et al (unpublished data, 2007) found that after ACL injury, joint unloading is associated with regional cartilage thinning. The lower joint moments and joint contact forces seen early after injury and ACLR in our subjects who went on to develop OA may be markers for underlying structural alterations to otherwise healthy articular cartilage before ACL injury. In our study, joint loading variables increased on the involved limb to levels similar to the nonOA group by 1 year after ACLR. Although it is unclear when early degenerative changes begin, the increase in loading at 2 years may not be tolerated if cartilage structures are already deconditioned or deteriorating. Further work is needed to determine whether the more symmetric loading present at 2 years will eventually lead to joint overloading as the degeneration progresses.

Seven of 22 patients demonstrated radiographic knee OA at 5 years after ACLR. A recent systematic review indicated that cartilage degeneration detected by magnetic resonance imaging (MRI) occurs before radiographic evidence.⁴⁷ Tibial cartilage thinning is evident on MRI as early as 4 months after isolated ACL injury,⁴⁶ and these changes persist despite ACLR.²⁵ The occurrence of preoperative articular cartilage changes highlights the importance of sufficient and purposeful rehabilitation before surgery. In the present study, despite resolution of knee joint effusion, ROM, pain, and obvious gait impairments, there were significant differences in frontal plane moments and also notable differences in medial compartment joint contact forces at baseline between subjects who later developed radiographic OA. All of these group differences were considerably smaller after an additional 10 rehabilitation sessions targeting further strength and neuromuscular improvements before surgery. It is likely that more subjects than the 7 in our study with radiographic OA exhibited early signs of cartilage degeneration. Weninger et al⁵⁵ reported that nearly 70% of patients demonstrated cartilage degeneration on MRI 2.8 years after ACLR but only 11% had radiographic knee OA. Early rehabilitation programs both before

and after ACLR may be a primary modifiable component to restore knee biomechanics and modify the course of early-onset knee OA.

The knee adduction moment was lower in the OA group when compared with both the contralateral limb and the involved limb of the nonOA group early after injury and surgery. Previous conflicting evidence regarding whether the knee adduction moment is increased or decreased after ACLR may be a result of failing to dichotomize ACL-injured subjects by the presence of later knee OA and to consider longitudinal changes in frontal plane loading after ACL injury. Webster and colleagues^{51,52} reported a lower knee adduction moment at 10 months after ACLR compared with both the contralateral limb and healthy controls, which improved at 3 years, which is consistent with current findings within the OA group in the present study. However, Webster et al⁵³ reported the absence of interlimb differences in the knee adduction moment at 20 months, while our 2-year results in the OA group show large between-limb differences for both the peak knee adduction moment and knee adduction moment impulse, consistent with 26-month findings by Zabala et al.⁵⁷ Previous research has reported that between 3.5 and 5.3 years after ACLR, patients have knee adduction moment values that are greater than, equal to, and less than those of healthy controls.^{5,39,48} Further analysis is required within our cohort to determine whether this period represents a critical time when a shift to overloading patterns becomes evident.

Significant differences in peak knee adduction moment and knee adduction moment impulse between the nonOA and OA group were present at baseline but not after preoperative rehabilitation. Subjects with OA demonstrated larger asymmetries between limbs in peak knee adduction moment and knee adduction moment impulse and lower knee adduction moment impulse on the involved limb at baseline, which normalized after rehabilitation. Meanwhile, the nonOA group walked with symmetric frontal plane moments at both points in time. Early identification of individuals at high risk of early-onset knee OA and determination of sufficient preoperative rehabilitation dosages may play a key role in curbing the unloading tendencies of certain individuals and potential pathway of irreversible knee joint OA.

Sagittal plane moments undoubtedly play a role in describing the loading environment of the knee's medial compartment.⁴⁹ Previous work has established that the peak knee flexion moment is lower both before and after ACLR.^{16,24,28,42–44,54,57} The negative interlimb differences in the peak knee flexion moment found for both the nonOA and OA groups at each time point further support this trend for involved limb unloading. Although only 7 of 22 subjects had radiographic knee OA at 5 years, the majority will likely develop radiographic knee OA within 15 years of surgery.³ It is possible that sagittal plane moments may be associated with overall long-term risk of knee OA while frontal plane moments may better differentiate subjects at risk of earlier radiographic knee OA present within 5 years of ACLR.

Six months after ACLR, differences between groups for both involved limb peak knee flexion moment and interlimb difference in peak knee flexion moment were not statistically significant, which is not consistent with the findings of others.^{24,42} The limited sample size in our current study may have restricted achievement of significant findings. However, large

effect sizes were present for both measures, suggesting that sagittal plane kinetics may also play a role in the early onset of knee OA.

Medial compartment joint contact forces estimated by use of an EMG-driven musculoskeletal model differed between subjects who did and those who did not develop radiographic knee OA at 5 years. An inherent strength of using this approach to describe the knee's loading environment is that it incorporates individual muscle activation patterns, which are known to be altered after ACL injury^{28,43,44} in addition to joint biomechanics. The OA group walked with lower medial compartment contact forces of the involved limb and large interlimb differences at baseline and 6 months after ACLR when compared with subjects without radiographic knee OA. Large differences between groups for the involved limb contact forces also persisted at 1 year. Previous work within this cohort found that medial compartment contact forces were significantly less in the injured limb before ACLR than in the contralateral limb.¹⁵ When these subjects were separated by the presence of knee OA at 5 years and their baseline data were analyzed, it was found that the involved medial compartment of the OA group was loaded nearly one-half BW less than the involved limb of the nonOA group at baseline. The OA group also had nearly an entire BW greater loading difference relative to the contralateral limb compared with the nonOA group at baseline. Again, these group differences were eliminated after additional preoperative rehabilitation. This relative unloading present in the OA group before and after surgery further highlights the key contributions that not only joint biomechanics but also muscle activation patterns may provide to the development of early knee OA. The more comprehensive approach undertaken by the musculoskeletal model to estimate joint loading, including the use of frontal and sagittal plane kinetics with co-contraction estimates via EMG input, may provide enhanced insight into the development of OA compared with kinetic measures alone. Further work is needed to determine whether relative contributions of muscle activation and joint biomechanics to joint contact forces differ between OA groups.

Concomitant meniscus and articular cartilage injuries increase the risk of degenerative changes in the knee after ACL injury.^{3,22,29,34,47} However, no subjects within either group possessed acute cartilage injury at the time of ACLR, and the proportion of meniscal injuries did not differ between subjects who did or did not go on to develop radiographic OA by 5 years. There were also no differences in the occurrence of additional knee injuries or surgery during the time from initial ACL injury to 5-year radiographic testing between those with and without OA at 5 years. The current findings do not refute previous findings regarding the increased OA risk associated with concomitant injuries. Given our findings, however, the strong association between biomechanical alterations and future knee joint degeneration can be attributed to ACL rupture independent of additional knee joint damage.

Previous studies reported that female sex increases the risk for development of primary knee OA,^{38,45} and it has been suggested that this risk factor may play a role in the risk of OA after ACL injury.³⁵ However, more recent studies have shown no risk factor of sex³ and further that male patients are at higher risk of knee OA after ACL injury.³⁴ Of our patients who completed testing at 2 years, a larger proportion of those who went on to demonstrate OA at 5 years were female (4 females, 1 male) compared with the nonOA group (2 females, 9 males). Women are more likely than men to demonstrate dynamic knee instability after

sustaining an ACL injury,²⁷ and within those subjects with poor dynamic stability, women demonstrate greater biomechanical asymmetries than men.⁹ The altered biomechanics in individuals with poor dynamic knee stability^{19,28} may place women at higher risk of early development of OA after ACL injury.

Age, obesity, and manual labor at the time of injury are additional factors that increase the risk of developing knee OA after ACL injury but are difficult to modify.^{3,34} Clinical signs such as muscle weakness have been linked to the development of primary knee OA, but modifiable risk factors related to knee OA after ACL injury are largely unknown.³⁵ The identification of clinical tests and measures that relate either to underlying altered joint biomechanics or directly to the development of knee OA after ACL injury are needed to effectively screen patients at greatest risk for posttraumatic OA, in whom targeted prevention strategies will be most effective.

Limitations do exist within the present study. Sample sizes are limited at each time point. The small sample size likely resulted in group differences that demonstrated large effect sizes but lacked statistical significance. Caution must be demonstrated in drawing firm conclusions from effect sizes when statistically significant group differences are not present, which warrants future study with the use of a larger sample. Further, some subjects were not tested at all time points, limiting further longitudinal analysis and chronological conclusions regarding loading patterns. Despite these limitations, it is important to note that this study is the first of its kind to demonstrate a link between altered movement patterns and radiographic evidence of knee OA after ACL injury. Further work is necessary to determine whether the presence of knee OA and altered knee joint biomechanics after ACL injury is also related to altered mechanics at the hip and ankle.

CONCLUSION

Patients with radiographic knee OA at 5 years after ACLR walked with lower knee adduction moments and medial compartment joint contact forces in the involved limb than did patients without OA early after injury and reconstruction. Knee joint loading became more similar between the groups at 1 year after ACLR. The time span between injury and 2 years after ACLR may represent a critical period during which articular cartilage health is highly sensitive to joint unloading and cartilage deconditioning. Further work is needed to determine effective rehabilitation strategies to both identify and amend these altered loading patterns associated with early-onset knee OA; in addition, research is needed to evaluate whether loading strategies differ greater than 2 years after ACLR between those who do and do not go on to develop radiographic knee OA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENT

The authors acknowledge Drs Wendy Hurd, Erin Hartigan, and Stephanie Di Stasi for their assistance with data collection.

source of funding: This work was supported by the National Institutes of Health (R01 AR048212, R01 AR046386, P30 GM103333).

REFERENCES

1. Adams D, Logerstedt DS, Hunter-Giordano A, Axe MJ, Snyder-Mackler L. Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression. *J Orthop Sports Phys Ther.* 2012; 42(7):601–614. [PubMed: 22402434]
2. Andriacchi TP, Koo S, Scanlan SF. Gait mechanics influence healthy cartilage morphology and osteoarthritis of the knee. *J Bone Joint Surg Am.* 2009; 91(suppl 1):95–101. [PubMed: 19182033]
3. Barenius B, Ponzer S, Shalabi A, Bujak R, Norlén L, Eriksson K. Increased risk of osteoarthritis after anterior cruciate ligament reconstruction: a 14-year follow-up study of a randomized controlled trial. *Am J Sports Med.* 2014; 42(5):1049–1057. [PubMed: 24644301]
4. Buchanan TS, Lloyd DG, Manal K, Besier TF. Neuromusculoskeletal modeling: estimation of muscle forces and joint moments and movements from measurements of neural command. *J Appl Biomech.* 2004; 20(4):367–395. [PubMed: 16467928]
5. Butler RJ, Minick KI, Ferber R, Underwood F. Gait mechanics after ACL reconstruction: implications for the early onset of knee osteoarthritis. *Br J Sport Med.* 2009; 43(5):366–370.
6. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences.* Hillsdale, NJ: Lawrence Erlbaum Associates; 1988. p. 567
7. Daniel DM, Stone ML, Dobson BE, Fithian DC, Rossman DJ, Kaufman KR. Fate of the ACL-injured patient: a prospective outcome study. *Am J Sports Med.* 1994; 22(5):632–644. [PubMed: 7810787]
8. Delp SL, Loan JP, Hoy MG, Zajac FE, Topp EL, Rosen JM. An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. *IEEE Trans Biomed Eng.* 1990; 37:757–767. [PubMed: 2210784]
9. Di Stasi SL, Snyder-Mackler L. The effects of neuromuscular training on the gait patterns of ACL-deficient men and women. *Clin Biomech.* 2012; 27:360–365.
10. Duffell LD, Southgate DFL, Gulati V, McGregor AH. Balance and gait adaptations in patients with early knee osteoarthritis. *Gait Posture.* 2014; 39:1057–1061. [PubMed: 24582072]
11. Fitzgerald GK, Axe MJ, Snyder-Mackler L. A decision-making scheme for returning patients to high-level activity with nonoperative treatment after anterior cruciate ligament rupture. *Knee Surg Sport Traumatol Arthrosc.* 2000; 8(2):76–82.
12. Foroughi N, Smith R, Vanwanseele B. The association of external knee adduction moment with biomechanical variables in osteoarthritis: a systematic review. *Knee.* 2009; 16:303–309. [PubMed: 19321348]
13. Frobell RB, Roos HP, Roos EM, Roemer FW, Ranstam J, Lohmander LS. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *BMJ.* 2013; 346:f232. [PubMed: 23349407]
14. Gardinier E, Di Stasi S, Manal K, Buchanan T, Snyder-Mackler L. Knee contact force asymmetries in patients who failed return-to-sport readiness criteria 6 months after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2014; 42(12):2917–2925. [PubMed: 25318940]
15. Gardinier E, Manal K. Altered loading in the injured knee after ACL rupture. *J Orthop Res.* 2013; 31:458–464. [PubMed: 23097309]
16. Gardinier ES, Manal K, Buchanan TS, Snyder-Mackler L. Gait and neuromuscular asymmetries after acute ACL rupture. *Med Sci Sport Exerc.* 2012; 44(8):1490–1496.
17. Gardinier ES, Manal K, Buchanan TS, Snyder-Mackler L. Minimum detectable change for knee joint contact force estimates using an EMG-driven model. *Gait Posture.* 2013; 38:1051–1053. [PubMed: 23601782]
18. Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. *J Rheumatol.* 2000; 27:1513–1517. [PubMed: 10852280]
19. Hartigan E, Axe MJ, Snyder-Mackler L. Perturbation training prior to ACL reconstruction improves gait asymmetries in non-copers. *J Orthop Res.* 2009; 27(6):724–729. [PubMed: 19023893]

20. Hartigan EH, Axe MJ, Snyder-Mackler L. Time line for noncopers to pass return-to-sports criteria after anterior cruciate ligament reconstruction. *J Orthop Sport Phys Ther.* 2010; 40(3):141–154.
21. Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. *Knee Surg Sport Traumatol Arthrosc.* 1993; 1(3–4):226–234.
22. Hirose J, Nishioka H, Okamoto N, et al. Articular cartilage lesions increase early cartilage degeneration in knees treated by anterior cruciate ligament reconstruction: T1ρ mapping evaluation and 1-year follow-up. *Am J Sports Med.* 2013; 41:2353–2361. [PubMed: 23925576]
23. Holm I, Oiestad BE, Risberg MA, Aune AK. No difference in knee function or prevalence of osteoarthritis after reconstruction of the anterior cruciate ligament with 4-strand hamstring autograft versus patellar tendon-bone autograft: a randomized study with 10-year follow-up. *Am J Sports Med.* 2010; 38(3):448–454. [PubMed: 20097928]
24. Hooper DM, Morrissey MC, Drechsler WI, Clark NC, Coutts FJ, McAuliffe TB. Gait analysis 6 and 12 months after anterior cruciate ligament reconstruction surgery. *Clin Orthop Relat Res.* 2002; 403:168–178. [PubMed: 12360023]
25. Hosseini A, Van De Velde S, Gill TJ, Li G. Tibiofemoral cartilage contact biomechanics in patients after reconstruction of a ruptured anterior cruciate ligament. *J Orthop Res.* 2012; 30:1781–1788. [PubMed: 22528687]
26. Hurd WJ, Axe MJ, Snyder-Mackler L. A 10-year prospective trial of a patient management algorithm and screening examination for highly active individuals with anterior cruciate ligament injury, part 1: outcomes. *Am J Sports Med.* 2008; 36(1):40–47. [PubMed: 17940141]
27. Hurd WJ, Axe MJ, Snyder-Mackler L. Influence of age, gender, and injury mechanism on the development of dynamic knee stability after acute ACL rupture. *J Orthop Sport Phys Ther.* 2008; 38(2):36–41.
28. Hurd WJ, Snyder-Mackler L. Knee instability after acute ACL rupture affects movement patterns during the mid-stance phase of gait. *J Orthop Res.* 2007; 25(10):1369–1377. [PubMed: 17557321]
29. Janssen RPA, du Mée AWF, van Valkenburg J, Sala HAGM, Tseng CM. Anterior cruciate ligament reconstruction with 4-strand hamstring autograft and accelerated rehabilitation: a 10-year prospective study on clinical results, knee osteoarthritis and its predictors. *Knee Surg Sport Traumatol Arthrosc.* 2013; 21:1977–1988.
30. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. *Ann Rheum Dis.* 1957; 16(4):494–502. [PubMed: 13498604]
31. Koo S, Andriacchi TP. A comparison of the influence of global functional loads vs. local contact anatomy on articular cartilage thickness at the knee. *J Biomech.* 2007; 40:2961–2966. [PubMed: 17418219]
32. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. *J Biomech.* 2007; 40:1754–1761. [PubMed: 17084845]
33. Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthritis Cartilage.* 2004; 12:745–751. [PubMed: 15325641]
34. 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. [PubMed: 22021585]
35. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med.* 2007; 35:1756–1769. [PubMed: 17761605]
36. Manal K, Buchanan TS. An electromyogram-driven musculoskeletal model of the knee to predict in vivo joint contact forces during normal and novel gait patterns. *J Biomech Eng.* 2013; 135:021014. [PubMed: 23445059]
37. Mündermann A, Dyrby CO, Andriacchi TP. Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis Rheum.* 2005; 52:2835–2844. [PubMed: 16145666]

38. Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, knee osteoarthritis among patients in a health maintenance organization. *Arthritis Rheum.* 1995; 38:1134–1141. [PubMed: 7639811]
39. Patterson MR, Delahunt E, Caulfield B. Peak knee adduction moment during gait in anterior cruciate ligament reconstructed females. *Clin Biomech.* 2014; 29:138–142.
40. Petersson IF, Boegård T, Saxne T, Silman AJ, Svensson B. Radiographic osteoarthritis of the knee classified by the Ahlbäck and Kellgren & Lawrence systems for the tibiofemoral joint in people aged 35–54 years with chronic knee pain. *Ann Rheum Dis.* 1997; 56:493–496. [PubMed: 9306873]
41. Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med.* 2007; 35(4):564–574. [PubMed: 17261567]
42. Roewer BD, Di Stasi SL, Snyder-Mackler L. Quadriceps strength and weight acceptance strategies continue to improve two years after anterior cruciate ligament reconstruction. *J Biomech.* 2011; 44(10):1948–1953. [PubMed: 21592482]
43. Rudolph KS, Axe MJ, Buchanan TS, Scholz JP, Snyder-Mackler L. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg Sport Traumatol Arthrosc.* 2001; 9(2):62–71.
44. Rudolph KS, Eastlack ME, Axe MJ, Snyder-Mackler L. 1998 Basmajian Student Award Paper: Movement patterns after anterior cruciate ligament injury: a comparison of patients who compensate well for the injury and those who require operative stabilization. *J Electromyogr Kinesiol.* 1998; 8:349–362. [PubMed: 9840891]
45. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage.* 2005; 13:769–781. [PubMed: 15978850]
46. Van De Velde SK, Bingham JT, Hosseini A, et al. Increased tibiofemoral cartilage contact deformation in patients with anterior cruciate ligament deficiency. *Arthritis Rheum.* 2009; 60:3693–3702. [PubMed: 19950260]
47. Van Ginckel A, Verdonk P, Witvrouw E. Cartilage adaptation after anterior cruciate ligament injury and reconstruction: implications for clinical management and research? A systematic review of longitudinal MRI studies. *Osteoarthritis Cartilage.* 2013; 21:1009–1024. [PubMed: 23685095]
48. Varma RK, Duffell LD, Nathwani D, McGregor AH. Knee moments of anterior cruciate ligament reconstructed and control participants during normal and inclined walking. *BMJ Open.* 2014; 4(6):e004753.
49. Walter JP, D’Lima DD, Colwell CW Jr, Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res.* 2010; 28(10):1348–1354. [PubMed: 20839320]
50. Webster KE, Feller JA. Alterations in joint kinematics during walking following hamstring and patellar tendon anterior cruciate ligament reconstruction surgery. *Clin Biomech.* 2011; 26:175–180.
51. Webster KE, Feller JA. The knee adduction moment in hamstring and patellar tendon anterior cruciate ligament reconstructed knees. *Knee Surg Sport Traumatol Arthrosc.* 2012; 20:2214–2219.
52. Webster KE, Feller JA, Wittwer JE. Longitudinal changes in knee joint biomechanics during level walking following anterior cruciate ligament reconstruction surgery. *Gait Posture.* 2012; 36:167–171. [PubMed: 22469773]
53. Webster KE, McClelland JA, Palazzolo SE, Santamaria LJ, Feller JA. Gender differences in the knee adduction moment after anterior cruciate ligament reconstruction surgery. *Br J Sports Med.* 2012; 46:355–359. [PubMed: 21508075]
54. Webster KE, Wittwer JE, O’Brien J, Feller JA. Gait patterns after anterior cruciate ligament reconstruction are related to graft type. *Am J Sports Med.* 2005; 33:247–254. [PubMed: 15701611]
55. Weninger P, Zifko B, Liska M, Spitaler R, Pelinka H, Hertz H. Anterior cruciate ligament reconstruction using autografts and double biodegradable femoral cross-pin fixation: functional, radiographic and MRI outcome after 2-year minimum follow-up. *Knee Surg Sport Traumatol Arthrosc.* 2008; 16:988–995.

56. Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. *J Biomech.* 2009; 42(14):2294–2300. [PubMed: 19647257]
57. Zabala ME, Favre J, Scanlan SF, Donahue J, Andriacchi TP. Three-dimensional knee moments of ACL reconstructed and control subjects during gait, stair ascent, and stair descent. *J Biomech.* 2013; 46:515–520. [PubMed: 23141637]
58. Zhao D, Banks SA, Mitchell KH, D’Lima DD, Colwell CW, Fregly BJ. Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. *J Orthop Res.* 2007; 25:789–797. [PubMed: 17343285]

Figure 1.
Flow diagram of study cohort. ACL, anterior cruciate ligament.

Figure 2.

Mean values for involved limb and interlimb differences in kinetic measures and medial compartment contact forces between those with and without radiographic medial compartment knee osteoarthritis (OA) 5 years after anterior cruciate ligament reconstruction. Effect sizes (ES) provided. * $P < .05$. Whiskers represent ± 1 standard deviation.

Demographic, Baseline, and Concomitant Injury Characteristics Between Those With and Without Radiographic Medial Compartment Knee OA 5 Years After ACLR^a

	Group	Baseline		Posttraining		6 Months		1 Year		2 Years	
		Mean ± SD	P	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P
Age (baseline), y	nonOA	33.42 ± 10.85	.868	33.80 ± 10.40	.983	32.50 ± 11.16	.062	32.90 ± 11.62	.309	35.18 ± 10.14	.463
	OA	34.67 ± 14.29		33.67 ± 13.74		44.75 ± 5.56		26.00 ± 8.76		39.60 ± 12.48	
Mass, kg	nonOA	86.59 ± 19.12	.351	86.06 ± 20.73	.936	86.84 ± 15.26	.238	89.41 ± 14.47	.727	87.70 ± 13.80	.338
	OA	75.03 ± 14.52		85.24 ± 17.11		76.33 ± 10.99		86.15 ± 17.96		80.25 ± 14.30	
Body mass index	nonOA	28.13 ± 3.69	.313	27.98 ± 3.91	.591	28.07 ± 2.94	.104	28.66 ± 4.15	.853	28.77 ± 3.04	.217
	OA	25.56 ± 4.30		29.13 ± 4.23		25.15 ± 2.37		28.16 ± 5.07		26.48 ± 3.83	
Time from injury to baseline, wk	nonOA	9.75 ± 8.30	.444	9.70 ± 9.16	.687	9.80 ± 7.17	.873	8.05 ± 7.08	.542	8.45 ± 7.31	.692
	OA	5.83 ± 2.25		11.58 ± 8.33		10.50 ± 7.38		10.88 ± 9.00		10.0 ± 6.49	
Time from injury to ACLR, wk	nonOA	18.82 ± 11.02	.189	18.89 ± 12.25	.916	15.20 ± 8.38	.422	19.30 ± 22.61	.709	19.82 ± 21.52	.941
	OA	9.67 ± 2.31		19.67 ± 15.67		21.00 ± 18.57		14.75 ± 9.18		19.00 ± 16.69	
Gait velocity, m/s	nonOA	1.57 ± 0.14	.592	1.60 ± 0.12	.418	1.61 ± 0.13	.320	1.64 ± 0.12	.035	1.62 ± 0.12	.226
	OA	1.52 ± 0.09		1.55 ± 0.10		1.54 ± 0.08		1.49 ± 0.04		1.54 ± 0.11	
Sex (male:female), n	nonOA	8:4	.077	7:3	.302	8:2	.095	8:2	.520	9:2	.036
	OA	0:3		2:4		1:3		2:2		1:4	
Preinjury activity level (I:II), ^b n	nonOA	6:6	>.999	6:4	.608	6:4	.085	7:3	.580	8:3	.106
	OA	1:2		2:4		0:4		2:2		1:4	
Graft type (allograft:autograft), n	nonOA	9:3	>.999	8:2	.299	8:2	.520	8:2	.520	10:1	.214
	OA	2:1		3:3		2:2		2:2		3:2	
Meniscal or articular cartilage concomitant injury (no:yes), n	nonOA	5:7	.200	5:5	.633	4:6	.559	3:7	.580	4:7	.282
	OA	3:0		4:2		3:1		2:2		4:1	
Medial tibiofemoral compartment concomitant injury (no:yes), n	nonOA	8:4	.516	7:3	>.999	7:3	>.999	7:3	>.999	7:4	>.999
	OA	3:0		5:1		3:1		3:1		4:1	
Additional knee injury after initial ACL injury (no:yes), n	nonOA	10:2	.516	9:1	.625	9:1	.714	9:1	.505	11:0	.313
	OA	2:1		5:1		4:0		3:1		4:1	

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

^a Boldfaced numbers indicate statistically significant baseline difference between those with and without radiographic medial compartment knee OA 5 years after ACLR ($P < .05$). ACL, anterior cruciate ligament; ACLR, ACL reconstruction; OA, osteoarthritis.

^b According to International Knee Documentation Committee activity levels.^{7,21}