Recovery of Running Biomechanics after Anterior Cruciate Ligament Reconstruction

By

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Dedication

This work is dedicated to my wife, Jacqueline. Without her selfless love and support this thesis would not have been possible. Graduate student life was full of ups and downs. There are periods of sprints, such as meeting a grant or conference abstract deadline. In these times it was a struggle to disconnect from the work and truly be present with family. Jacqueline's understanding and patience were greatly appreciated during these stressful moments. There were periods of failures, such as not receiving a grant, getting a manuscript rejection, or struggling for hours to generate a figure I envisioned. Jacqueline consistently provided perspective and consoled me in these times of frustration. There were periods of success, such as receiving grants, getting manuscripts published, being selected for awards, or creating that figure on the first try. Jacqueline was always the first person I wanted to tell, and has been my biggest fan. To Jacqueline, I cannot thank you enough for all your support.

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I would like to thank all the committee members for their time and dedications to providing me feedback and guidance in completion of this thesis. Additionally, the work presented in this thesis was undoubtedly a team effort from the Badger Athletic Performance Team. Thank you Jen, Mikel, Christa, Jack, Scott, Liz, Claire, Courtney, and Herman for supporting this work in a multitude of ways. Moreover, I would like to thank the undergraduate and graduate students that entrusted me as a research mentor and assisted me on various projects throughout my graduate studies. Lastly, I would like to acknowledge the Athletics Sports Medicine staff and the student athletes themselves. Without everyone’s buy in to the Badger Athletic Performance program, this work would not be possible.

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Abstract

Background: Anterior cruciate ligament (ACL) injuries are traumatic for young athletes and typically lead to surgical reconstruction (ACLR) followed by extensive rehabilitation. Athletes commonly demonstrate altered biomechanics during running post-ACLR. Persistent abnormalities in mechanics have been implicated as a mechanism of post-ACLR osteoarthritis. The purpose of this thesis was to investigate the longitudinal recovery of running biomechanics and the relationship to quadriceps performance and bone health.

Methods: Healthy baseline and post-ACLR data from the Badger Athletic Performance database (2011 to 2022) were utilized. Chapter 1 leveraged preinjury running data to describe changes in running mechanics over the first 12 months post-ACLR. Chapter 2 characterized the effect of running speed on knee biomechanics between 4-7 and 8-12 months post-ACLR. Chapter 3 assessed the relationship between recovery in running biomechanics and quadriceps performance 3-24 months post-ACLR. Chapter 4 explored the influence knee biomechanics during running and quadriceps performance have on bone mineral density between 3-24 months post-ACLR.

Results: Athletes demonstrated persistent deficits in surgical knee biomechanics during running post-ACLR compared to preinjury. Running speed and quadriceps performance were associated with changes in knee biomechanics, but neither fully resolved running asymmetries. Greater recovery of quadriceps rate of torque development post-ACLR was associated with less bone loss.

Conclusion: This thesis highlights persistent abnormalities in knee biomechanics during running following ACLR, identifies quadriceps performance and running speed as potential modifiable factors associated with running mechanics, and suggests that restoring quadriceps rate of torque development early and completely may help to minimize bone loss post-ACLR.

Introduction

Anterior cruciate ligament (ACL) injuries are devastating for young athletes, not because of the initial trauma, but rather the permanence of deficits.[18,28,127] Long-term impairments in knee mechanics, quadriceps performance, and neurophysiological function have been documented in individuals following ACL reconstruction (ACLR).[32,59,87,91,92,127] These deficits likely contribute to decreased physical activity, persistent pain, reduced quality of life, increased risk for early onset osteoarthritis (OA), and a lifetime societal healthcare burden estimated at $7.6 billion annually.[29,74,127] Post traumatic knee osteoarthritis is of particular concern following ACLR as 50-90% of patients demonstrate signs of OA later in life compared to 12% in the general population.[37,70,142] Additionally, increased prevalence of total knee arthroplasty in individuals following ACLR has been observed, particularly at younger ages.[1,84,114]

Altered knee mechanics have been suggested to contribute to this increase in post-traumatic knee osteoarthritis,[3,17] but current evidence is limited to walking[99,146] or animal models.[147] As the majority of athletes have return-to-sport (RTS) aspirations following ACLR, running is a primary component of their rehabilitation. Additionally, individuals that elect not to return to organized sport may use running as a way to maintain an active, healthy lifestyle.[33] Running introduces significantly greater joint contact forces than walking in healthy individuals.[79] As such, altered running mechanics and knee cartilage loads may contribute to the increased prevalence of post-traumatic knee osteoarthritis following ACLR. A first step in this line of inquiry is to better understand the longitudinal changes in running knee mechanics after ACLR.

Another major concern post-ACLR is that only 65% of athletes return to their prior level of sport and only 55% return to a competitive level.[4] Of those that do return, re-injury rates have been reported as high as 30%.[148] Successfully returning to sport was found to be the strongest predictor of a high self-reported quality of life in individuals 5-20 years post-ACLR. Those that did not return had higher BMI, more contralateral ACL injuries, and more knee surgeries.[28] Therefore, identifying factors that contribute to the poor RTS rates and high re-injury rates is a crucial next step in improving outcomes following ACLR. Current RTS testing typically includes quadriceps strength assessment, in-clinic functional testing, and patient-reported outcomes, aiming for less than a 10% deficit compared to the non-surgical limb on all tests to demonstrate RTS readiness.[78] Despite employing this standard testing battery, there is minimal indication that it reduces re-injury risk, supporting the notion that current RTS testing may be missing integral components.[68,144] In fact, sagittal plane knee joint mechanics of the non-surgical limb were recently found to identify those at risk for a subsequent ACL injury when common symmetry measures were not.[50] Better understanding deficits in sport-specific movement mechanics of both limbs and quadriceps performance beyond simply strength may highlight missing aspects of current RTS testing.

A growing body of evidence has focused on the impact ACL injury and ACLR has on lower extremity bone mineral density (BMD).[88] Lower extremity BMD deficits have been observed in both the short- (less than 1 year)[25,60,71,82] and long-term (10-11 years) following ACLR.[46] Significant BMD deficits have been documented at the proximal tibia, distal femur, patella, proximal femur or hip region, and calcaneus of the involved limb following ACLR.[88] More recently, longitudinal studies found significant reductions in BMD compared to pre-surgery at the distal femur and proximal tibia, which persisted 2 years post-operative.[77,82] Despite these being large longitudinal studies, the populations varied in physical activity levels and the findings may not generalize to high-level athletes. Reduced subchondral BMD, particularly surrounding the knee, has been associated with the development of OA in the general population.[8] Therefore, bone loss following ACLR may be an important metric to consider as a precursor to the development of OA in these individuals.[18,19,111] Moreover, it is plausible that such bone loss increases periprosthetic fracture risk following total knee arthroplasty,[55] which is unfortunately common in individuals long after ACLR.[1,84,114] It remains unknown what factors contribute to bone loss, but it has been postulated that reduced activity levels and/or reduced mechanical loading during tasks such as walking, running, and jumping may contribute to this deficit.[88]

Returning to running following ACLR is a key rehabilitation milestone for many athletes, particularly for those interested in returning to sport. Further, individuals without RTS aspirations may elect to use running as a way to maintain an active lifestyle.[33] Current clinical practice for clearing athletes to return to run is based primarily on time post-operatively with the most common time frame of clearance being 12-16 weeks post-ACLR.[106] A scoping review highlighted that the objective criteria, beyond time post-operatively, reported in the literature varies widely.[106] This review provided suggestions of criteria to consider when returning athletes to running post-ACLR, including: knee flexion range of motion (>90% other side), knee extension range of motion (full), knee joint effusion (trace or less), pain (<2/10 on the visual analog scale), quadriceps strength (60-80% limb symmetry index (LSI)), single limb support (single leg balance), functional tests (hop variations >70% LSI), and others.[106] However, these recommendations are based solely on expert opinion and/or what has been reported in the literature, with little to no primary evidence to support the specific recommendations or cutoffs.

Common questions patients and physical therapists have in regard to running post-ACLR include: “When is it safe to run post-ACLR?” or “What physical capacities are required to run post-ACLR?” Unfortunately, these questions are not easily answered. While this thesis does not directly answer this question, findings from this work may provide some insight into what physical capacities are necessary to run without substantial asymmetries. Further, assessing changes in knee biomechanics of both limbs from preinjury to 1 year post-ACLR can help determine the appropriateness of using the non-surgical limb as a reference for comparison throughout rehabilitation. If minimal changes are observed in the non-surgical limb compared to preinjury, the non-surgical limb can serve as a valid reference when preinjury data is not available. Moreover, these data can help demonstrate if simply exposing an athlete to running leads to improvements in running symmetry.

It is important to highlight that the data included in this dissertation comes from a clinical database; therefore, the post-ACLR rehabilitation management reflects what commonly occurs in clinical practice. Most athletes included in this dissertation resumed running between 3-4 months post-operatively, which is consistent with the current literature.[106] In addition, quadriceps performance metrics varied widely, particularly early post-operatively (3-6 month quadriceps strength LSI 63% ± 18). Having running data ranging from 3-24 months post-ACLR paired with a large distribution of quadriceps performance data enhances the ability to explore associations between quadriceps performance and running mechanics.

To date, most of the ACL literature relating to running biomechanics, quadriceps performance, or bone health after ACLR has considered each of these factors independently, neglecting the potential interactions between each factor. Further, it is unknown how running speed influences running mechanics following ACLR. Running speed may be an important confounder to consider from a research perspective, and it may be a simple, modifiable factor that can be prescribed clinically to improve running biomechanics in athletes following ACLR. The following subsections describe the current state of knowledge pertaining to running, quadriceps performance, and bone health in individuals following ACLR and establish the need for the studies presented in the subsequent chapters.

Alterations in Running Mechanics Post-ACLR

A systematic review and meta-analysis from 2019 assessed common alterations in running biomechanics in individuals following ACLR.[92] Observational studies were included that assessed running kinematics, kinetics, and/or muscle activation. Studies ranged from 3 months[47] to 5 years post-ACLR.[10,87] Compared to the non-surgical limb and healthy controls, surgical knee mechanics during running had significant reductions in peak knee flexion angles, knee flexion excursion, and knee extensor moments, based on the meta-analysis results.[92] For variables that were not reported consistently or had significant heterogeneity in methodology between studies (internal knee abduction moment, patellofemoral joint contact force, tibiofemoral joint contact force, and muscle activation), there was limited and mixed evidence for the directionality of a difference as compared to the non-surgical or healthy controls.

A significant limitation to the current state of literature surrounding running biomechanics post-ACLR is that the majority of studies are of cross-sectional design. Due to the ease of measuring both the surgical and non-surgical limb, most researchers and clinicians use between-limb comparisons for the assessment of recovery of biomechanics and quadriceps neuromuscular performance post-ACLR. Using the non-surgical limb as a reference may be invalid as bilateral changes have been observed post-ACLR.[59,95,145] Although using a healthy control group addresses the issue of non-surgical limb changes, it requires an increased recruitment burden and it is likely necessary to match controls on factors such as body mass index, age, and sex. Having access to an individual's preinjury running mechanics provides an ideal, within-athlete reference and enable researchers to assess changes in both the surgical and non-surgical limbs. Due to the total number of athletes needed to be tested preinjury to obtain a large enough sample to make inferences, this type of information is extremely rare and typically, when available, is only from a single case.[120–122] The Badger Athletic Performance program has been collecting pre-season running mechanics as part of the performance testing from all athletes in high-risk sports over the past decade. Identifying persistent biomechanical deficits compared to preinjury may help guide future clinical trials attempting to resolve these deficits with the goal of improving RTS rates, reducing re-injury risk, and reducing the onset and progression of post-traumatic knee osteoarthritis.

Running and Quadriceps Neuromuscular Performance

Restoration of quadriceps strength is an integral component of rehabilitation following ACLR and is commonly used to guide exercise progression and return to sport.[2] For the entirety of this dissertation, quadriceps performance is in reference to both quadriceps strength (maximal isometric knee extensor torque) and rate of torque development. Clinically, quadriceps performance is almost exclusively assessed via quadriceps strength due to the simplicity of the measure and its inclusion in standard reports generated by isokinetic dynamometer software. Rate of torque development is more challenging to assess in a clinical setting, requiring a rigid system, low signal-to-noise ratio, and a high sampling rate.[73] Additionally, there are many options for characterizing rate of torque development (e.g. as the peak slope, from contraction onset within a specified interval, or the time to reach a specified torque output), with no consensus on the most clinically relevant method.[73] As such, research investigating the relationship between quadriceps performance and movement mechanics is heavily focused on quadriceps strength.

Previous studies have explored the relationship between quadriceps performance deficits and alterations in running gait biomechanics post-ACLR.[7,51,95] These studies reported wide variations in the relationship between quadriceps performance and running mechanics, but they generally found a positive relationship. This prior work is significantly limited due to cross-sectional design as well as assessing quadriceps strength and/or rate of torque development independently. There is a need for longitudinal assessment of both quadriceps performance and running biomechanics to identify clinically relevant quadriceps performance metrics to target in an attempt to restore running biomechanics following ACLR.

Running and Bone Health

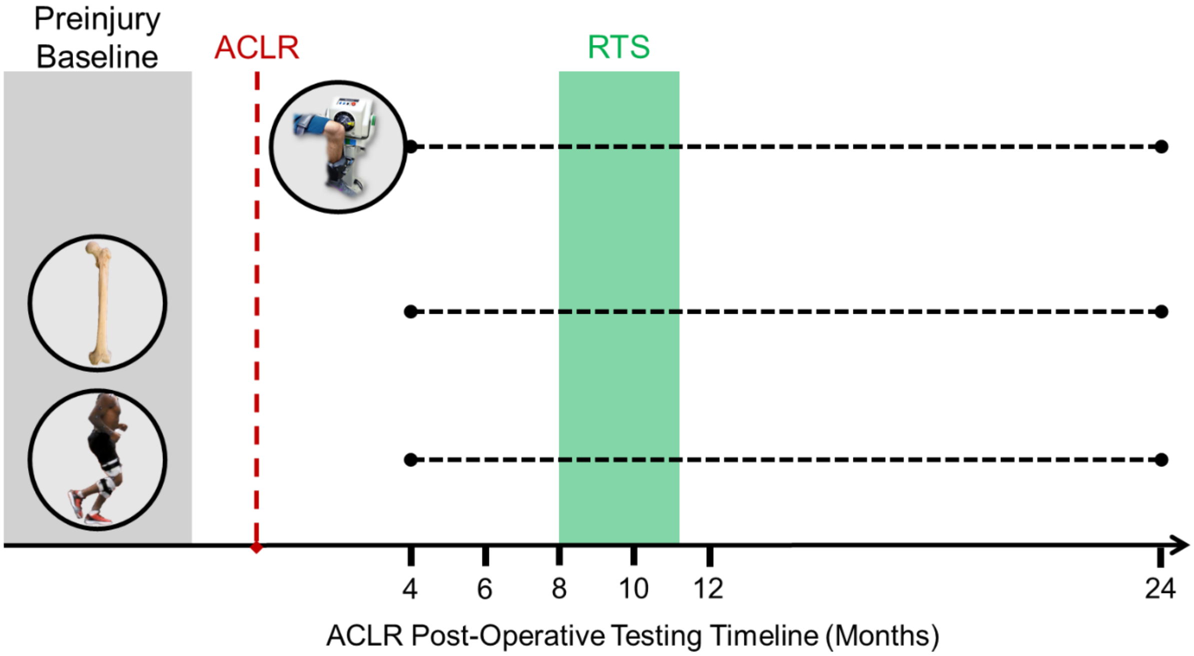
In addition to preinjury running mechanics, our lab collects BMD data as part of healthy, baseline performance testing via dual-energy X-ray absorptiometry (DXA) scans. In athletes that went on to sustain an ACL injury and undergo subsequent reconstruction, we paired healthy preinjury DXA scans with post-operative DXA scans. Using this unique dataset, we assessed longitudinal changes in BMD over the first 2 years post-ACLR in Division I collegiate athletes as compared to the preinjury state.[53] We found significant deficits focal to the distal femur (15% of femur length) that persisted to 24 months post-ACLR.[53] Prior work has demonstrated deficits in femur BMD in the long-term post-ACLR,[88] but this was the first study to compare to preinjury values in NCAA Division I collegiate athletes, most of whom returned to full sports participation. However, it remains unknown what factors may influence the deficits in BMD observed. It has been suggested that variations in activity levels and/or mechanical loading of the distal femur contributes to this bone loss.[88] Altered running mechanics may result in a chronic underloading of the distal femur, leading to or contributing to persistent bone loss.[24] Further, the quadriceps generates compressive and shear forces about the distal femur.[75] As such, persistent deficits in quadriceps strength and rate of torque development, which is common,[65,141] may impact bone loss post-ACLR.

Organization of the Dissertation

This dissertation leveraged the unique longitudinal data available from the Badger Athletic Performance database to address the primary objective of identifying the relationships of running biomechanics with quadriceps performance, bone health, running speed, and time (Figure 1). Chapter 1 highlights the impact ACL injury and subsequent surgery has on running biomechanics by assessing the longitudinal changes in running biomechanics from preinjury to 1 year post-operatively. Chapter 2 characterize how knee biomechanics change with running speed at two clinically relevant time points (shortly after initiating running and close to the time of return to sport). Chapter 3 assesses the relationship between recovery in quadriceps performance (isometric peak torque and rate of torque development) and the recovery in knee biomechanics during running over the first 2 years post-ACLR. Lastly, chapter 4 assesses the relationship of quadriceps performance and knee biomechanics during running with changes in distal femur BMD over the initial 2 years post-operatively.

Figure 1. Badger Athletic Performance post-anterior cruciate ligament reconstruction (ACLR) objective testing data included in this thesis. Preinjury dual-energy X-ray absorptiometry (DXA)

scans and running mechanics are collected as part of healthy team testing. Post-ACLR data utilized for this dissertation includes running, DXA, and isometric quadriceps performance analyses between 3 and 24 months post-ACLR. RTS, return to sport.



Chapter 1. Running Biomechanics Before Injury and 1 Year After Anterior Cruciate Ligament Reconstruction in Division I Collegiate Athletes

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Abstract

Background: Pre-injury running biomechanics are an ideal comparator for quantifying recovery of running biomechanics following anterior cruciate ligament reconstruction (ACLR), allowing for assessments within both the surgical and non-surgical limbs. However, availability of pre-injury running biomechanics is rare and has only been reported in case studies.

Hypothesis/Purpose: To determine if running biomechanics return to pre-injury levels within the first year post-ACLR among collegiate athletes. We hypothesized that surgical knee biomechanics would be significantly reduced shortly after ACLR and not return to pre-injury levels by 12 months, and non-surgical limb mechanics would change significantly from pre-injury.

Study Design: Analysis of routinely collected athletic performance data; Level of Evidence, 3.

Methods: Thirteen Division I collegiate athletes were identified between 2015 and 2020 (6 female; 20.7±1.3 years old) who had whole body kinematics and ground reaction forces recorded during treadmill running (3.7 ± 0.6 m/s) prior to sustaining an ACL injury. Running analyses were repeated at 4 (4M), 6 (6M), 8 (8M), and 12 (12M) months post-ACLR. Linear mixed effects models were used to assess differences in running biomechanics between post-ACLR time-points and pre-injury within each limb, reported as Tukey-adjusted p-values.

Results: Compared to pre-injury, the surgical limb displayed significant deficits at all post-operative assessments (p-values <0.01, reported as least square mean difference ± standard error): peak knee flexion angle (4M: 13.2°±1.4, 6M: 9.8°±1.4, 8M: 9.7°±1.4, 12M: 9.0°±1.5); peak knee extensor moment (4M: 1.32±0.13, 6M: 1.04±0.13, 8M: 1.04±0.13, 12M: 0.87±0.15 Nm/kg; 38 to 57% deficit); and rate of knee extensor moment (4M: 22.7±2.4, 6M: 17.9±2.3, 8M: 17.5±2.4, 12M: 16.1±2.6 Nm/kg/s; 33 to 46% deficit). No changes for these variables from pre-injury (p-values > 0.88) were identified in the non-surgical limb.

Conclusion: Following ACLR, surgical limb knee running biomechanics were not restored to the pre-injury state by 12M, while non-surgical limb mechanics remained unchanged compared to pre-injury.

Clinical Relevance: Collegiate athletes post-ACLR demonstrate substantial deficits in running mechanics compared to pre-injury that persist beyond the typical return-to-sport timeframe. The non-surgical knee appears to be a valid reference for recovery of the surgical knee mechanics during running, due to the lack of change within the non-surgical limb.

Introduction

Following anterior cruciate ligament reconstruction (ACLR), athletes demonstrate significant alterations in surgical limb running biomechanics compared to both their non-surgical limb and healthy controls.[92] These changes include: decreased peak knee flexion angle[48,92] and knee flexion excursion,[92] decreased peak knee extensor moment,[48,92,97] decreased patellofemoral joint force,[132] increased initial impact forces,[87] and decreased peak vertical ground reaction force.[97] Compensatory loading strategies, particularly at the hip,[9,87] have also been observed, indicating changes extend beyond the knee joint. Running asymmetries have been observed up to 5 years post-operatively, despite rehabilitation typically ending 6-12 months post-surgery.[87] Persistent alterations in movement mechanics and knee joint loading may contribute to the early onset and progression of knee osteoarthritis after ACLR.[3,17,132] Understanding the longitudinal changes in running biomechanics during the initial year following ACLR, when athletes typically have access to rehabilitation, is a necessary step toward identifying appropriate strategies aimed at improving running deficits in hopes of mitigating the sequela of joint disease.

Previous studies of running mechanics post-ACLR have used cross-sectional designs where the non-surgical limb or healthy controls are used for comparison.[92] The appropriateness of using the non-surgical limb as a comparative reference has come into question due to the potential for bilateral neuromuscular and biomechanical performance deficits to be present after injury and/or surgery.[59,95,145] For example, changes in walking mechanics have been observed over time in the non-surgical limb following ACLR.[26] As such, the appropriateness of using the non-surgical limb as a reference to evaluate recovery of the surgical limb must be assessed, particularly with regard to running mechanics.

To this end, one must compare longitudinal post-operative data with pre-injury data, allowing for bilateral assessment of within-limb changes over time. Baseline pre-injury data are not commonly available due to the unpredictable nature of ACL injures.[81] To date, only a few case studies have been published comparing pre-injury and post-operative running mechanics with limited generalizability.[120,121] Preseason assessments of running biomechanics among collegiate athletes at the University of Wisconsin-Madison have established a database of healthy baseline measures on hundreds of athletes. In the event an athlete suffers an ACL injury, the pre-injury baseline provides a unique reference for determining post-operative changes in the surgical and non-surgical limbs.

The purpose of this study, therefore, was to assess the longitudinal changes in running biomechanics throughout the first year post-ACLR compared to the pre-injury state among National Collegiate Athletic Association (NCAA) Division I collegiate athletes. We hypothesized that knee joint kinematics and kinetics and ground reaction forces (GRF) of the surgical limb during running would be significantly reduced shortly after ACLR and not return to the pre-injury state by 12-months. Additionally, we hypothesized that the non-surgical limb kinematics, kinetics, and GRF would change significantly from the pre-injury assessment. Finally, we explored longitudinal changes in hip and ankle joint kinetics (i.e., negative work).

Materials and Methods

Participants

Six years (2015-2020) of routinely collected pre-season performance data and post-ACLR testing available on NCAA Division I athletes in the University of Wisconsin-Madison Badger Athletic Performance database were used for this study (329 unique athletes with baseline running analyses). The record review was approved by the University's Health Sciences Institutional Review Board. Records were included if the athlete: 1) had an ACL injury and underwent a primary ACLR; 2) had no history of a previous ACL injury on either limb, 3) had a healthy, pre-injury running gait analysis and at least one post-operative running gait analysis; and 4) did not have a lower extremity surgery 12 months prior to the pre-injury running analysis. For athletes that met all of the above criteria, but sustained a second ACL injury or underwent a subsequent lower extremity surgery any time after the initial post-operative running gait analysis, only running gait analyses prior to these injuries were included.

Data Collection and Analysis

The running mechanics collection protocol utilized has been described in detail previously.[135] In brief, athletes walked for two minutes to acclimate to the treadmill and motion capture setup. For healthy baseline testing, athletes ran at standardized speeds of 2.68, 2.95, 3.35, 3.80, and 4.47 m/s (10, 9, 8, 7, and 6 min/mile, respectively). Following ACLR, athletes underwent a standardized testing protocol which included running gait analyses performed at 4, 6, 8, and 12 months post-operatively. During post-ACLR testing, speed was increased incrementally, following a similar progression to baseline testing, and athletes were asked to identify when they felt they achieved their maximally comfortable speed; testing was ended following collection of that speed. Fatigue was not directly assessed, but athletes were advised to verbalize if they were feeling fatigued. If fatigue was reported, speed was reduced to a walking pace until the athlete reported readiness to commence running. Fifteen seconds of data were recorded at each running speed after the athlete had acclimated to the speed for at least 30 seconds. Speed was controlled within each athlete by analyzing the maximum speed available that was consistent across all time points (pre-injury and post-ACLR), but speed was allowed to vary between athletes.

Whole-body kinematics were collected using 42 reflective markers placed on the body segments of each athlete, 23 of which were located on anatomical landmarks.[38] Markers were placed by the same researcher [MRSJ] for all data collections on all athletes. A static standing position was also recorded to establish joint centers and for model scaling. Marker kinematics were collected at 200 Hz using an 8-camera passive marker system (Motion Analysis Corporation, Santa Rosa, CA). Ground reaction forces were recorded at 2000 Hz using an instrumented treadmill (Bertec Corporation, Columbus, OH) and synchronized with the kinematic marker data. To identify foot contacts and calculate GRF metrics, the GRFs were low-pass filtered using a bi-directional, 3rd-order Butterworth filter with a cutoff frequency of 50 Hz.[135] Gait cycles were identified by foot contacts, with the stance phase of the gait cycle defined from initial contact to toe off, when the vertical GRF rose above and fell below 50 N, respectively.

Biomechanical modeling and analyses have been described in detail.[38] Briefly, the body was modeled as a 14-segment articulated linkage and body segments were scaled using the athlete's height, mass, and segment lengths.[62] Joint angles were computed at each time step using a global optimization routine to minimize the weighted sum of squared differences between the measured and the model marker positions.[69] In addition, a segment-by-segment inverse dynamics analysis was used to calculate joint moments from the kinematic data and GRFs, both low-pass filtered using a bi-directional, 4th-order Butterworth filter at 12 Hz. Joint powers were computed as the product of the moment and angular velocity for each joint, with mechanical work determined by numerically integrating the respective portions of each joint power curve.

Fifteen strides were analyzed on both limbs from each athlete and included the following biomechanical variables: peak knee flexion during stance; peak knee extensor moment during stance; rate of knee extensor moment during stance; hip, knee, ankle, and total negative work during stance (summation of hip, knee, and ankle negative work); vertical GRF impulse; and braking impulse. All signal and data processing were conducted using MATLAB (Release 2018b, Mathworks, Inc., Natick, MA).

Statistical Analysis

Standard descriptive statistics (means/standard deviations and frequencies/percentages) were used to describe the patient population. Linear mixed effects models were used to assess the influence of time-point and limb, and a potential interaction effect, on each biomechanical variable of interest. Subject and limb were assigned as random effects. For variables in which a significant interaction was detected, Tukey-adjusted p-values were used for pairwise comparisons between pre-injury and post-operative time-points for the surgical and non-surgical limb separately. Speed was controlled within each athlete by using the maximum speed that was consistent across all collections for that athlete; however, due to the small sample size between-athlete variability due to speed was not assessed. Least-square mean differences and associated standard errors are reported. All analyses were conducted using SAS v9.4 (SAS Institutes, Cary, NC) and significance was assessed at $\alpha \leq 0.05$.

Results

Records for 13 athletes met eligibility criteria and were included in the final dataset (Figure 1.1). All athletes underwent ACLR with bone-patellar-tendon-bone autograft. Five athletes underwent ACLR only, 3 underwent ACLR + meniscectomy, and 5 underwent ACLR + meniscus repair. Athletes participated in football (7), basketball (2), soccer (3), or track and field (1). All athletes completed a pre-injury running analysis (14.6 ± 11.9 months prior to surgery). Post-operatively, 9, 10, 9, and 7 athletes completed testing at 4, 6, 8, and 12 months, respectively. One athlete sustained a contralateral ACL injury (10-months post-op) and two others underwent additional lower extremity surgeries (5 and 7 months post-op). The majority of the athletes (9/13 athletes) in our study started running between 3 and 4 months post-surgery. The average speed used for comparisons was 3.65±0.59 m/s (7:20 min/mile) and no athletes reported fatigue during testing. Additional patient demographics appear in Table 1.1.

Figure 1.1. Records extraction process. All athletes included in the analysis had running data from pre-injury and at least one post-operative time point. ACL, anterior cruciate ligament.

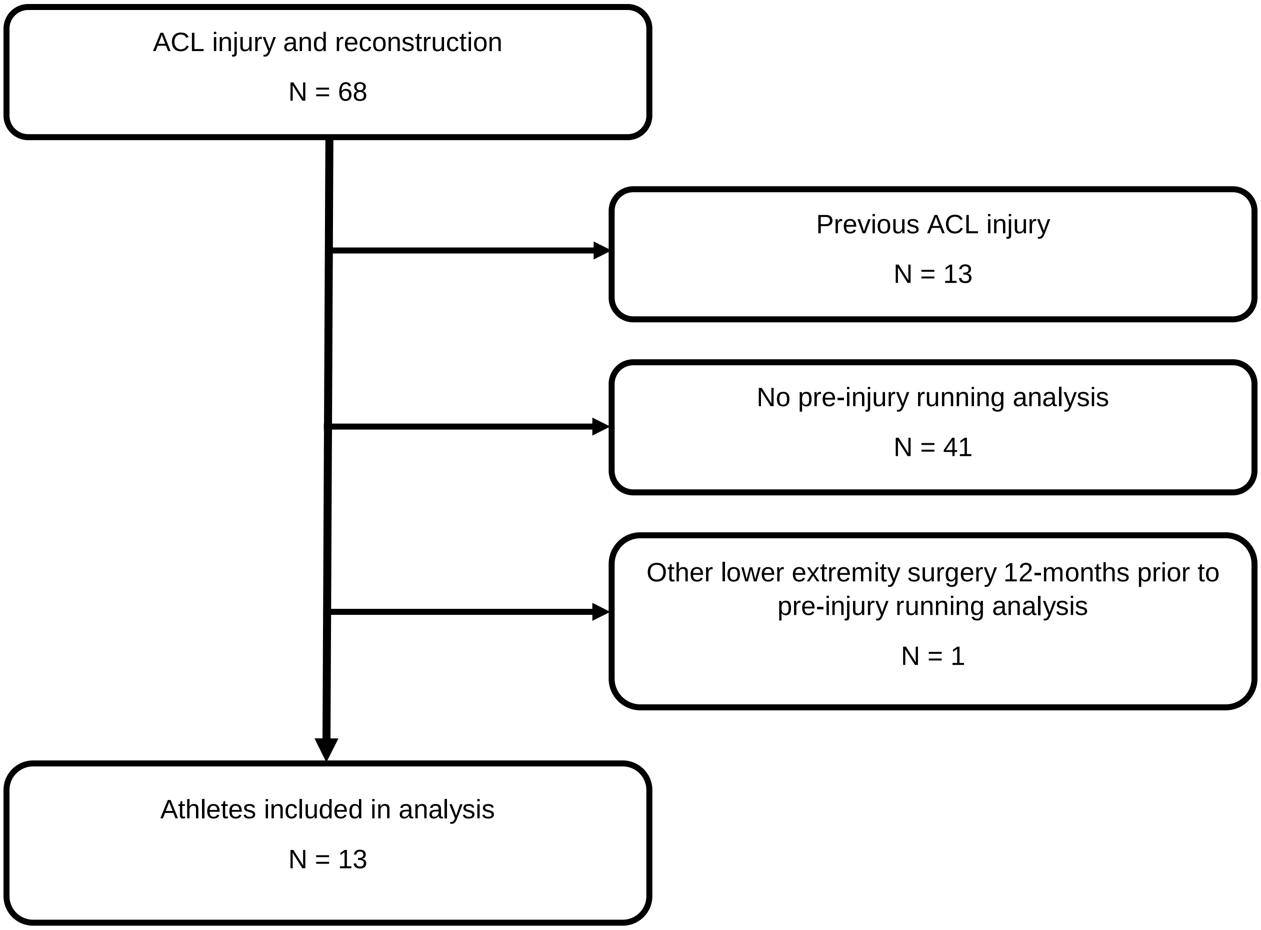

ACL injury and reconstruction
N = 68
Previous ACL injury
N = 13
No pre-injury running analysis
N = 41
Other lower extremity surgery 12-months prior to pre-injury running analysis
N = 1
Athletes included in analysis
N = 13

Table 1.1. Summary of participant information.

Participant Information (N = 13)[a]	
	Values
Age, y*	20.7 ± 1.3
Body Mass, kg*	84.7 ± 18.5
Height, cm*	179.3 ± 8.9
Females, n (% of total participants)	6 (46)
Running Speed, m/s	3.65 ± 0.59
Running Analysis From Time of ACLR, mo	
Pre-injury	14.6 ± 11.9
4-month	3.9 ± 0.4
6-month	6.1 ± 0.3
8-month	8.4 ± 0.8
12-month	12.2 ± 1.3
IKDC, %	
4-month	62.6 ± 18.7
6-month	75.3 ± 14.4
8-month	90.3 ± 7.2
12-month	91.0 ± 14.3

[a] Values are presented as mean ± SD unless otherwise indicated. *Based on 4-month post-operative assessment. ACLR, anterior cruciate ligament reconstruction IKDC, International Knee Documentation Committee survey.

A significant time*limb interaction was detected for peak knee flexion angle, peak knee extensor moment, rate of knee extensor moment, and knee negative work (all p-values<0.001). No significant changes in the non-surgical limb knee biomechanics compared to pre-injury were identified throughout the first 12 months post operatively (Figure 1.2, Table 1.2); however, the surgical knee demonstrated significant reductions in all of these metrics at all time-points compared to pre-injury (all p-values<0.001; Table 1.2). The largest deficits (indicated by the negative sign) in the surgical knee mechanics compared to pre-injury mechanics were observed at 4 months and did not return to pre-injury levels by 12 months [peak knee flexion angle: 4-months = -13.2°±1.4 (p<0.001), 12-months = -9.0°±1.5 (p<0.001); peak knee extensor moment: 4-months = -1.32±0.13 Nm/kg (p<0.001), 12-months = -0.87±0.15 Nm/kg (p<0.001); rate of knee extensor moment: 4-months = -22.7±2.4 Nm/kg/s ($p<0.001$), 12-months = -16.1±2.6 Nm/kg/s ($p<0.001$)]. All time-points are reported in Figure 1.2 and Table 1.2. Knee negative work was significantly reduced at all follow-up time-points within the surgical limb (4 months: -0.33±0.04 J/kg, $p<0.001$; 6 months: -0.27±0.04 J/kg, $p<0.001$; 8 months: -0.25±0.04 J/kg, $p<0.001$; and 12 months: -0.22±0.05 J/kg, $p=0.002$) (Figure 1.3).

Figure 1.2. Least-square mean values of peak knee flexion angle during stance (top), peak knee extensor moment during stance (middle), and rate of knee extensor moment during stance (bottom) from pre-injury (PRE) to 12-months post-anterior cruciate ligament reconstruction (ACLR) within the surgical (black) and non-surgical limb (grey). Error bars depict the standard error of the least-square mean. The axis break between pre-injury and 4-months demonstrates that the time interval between pre-injury and 4-months varies between participants. *** Significant within-limb difference from pre-injury $p < 0.001$.

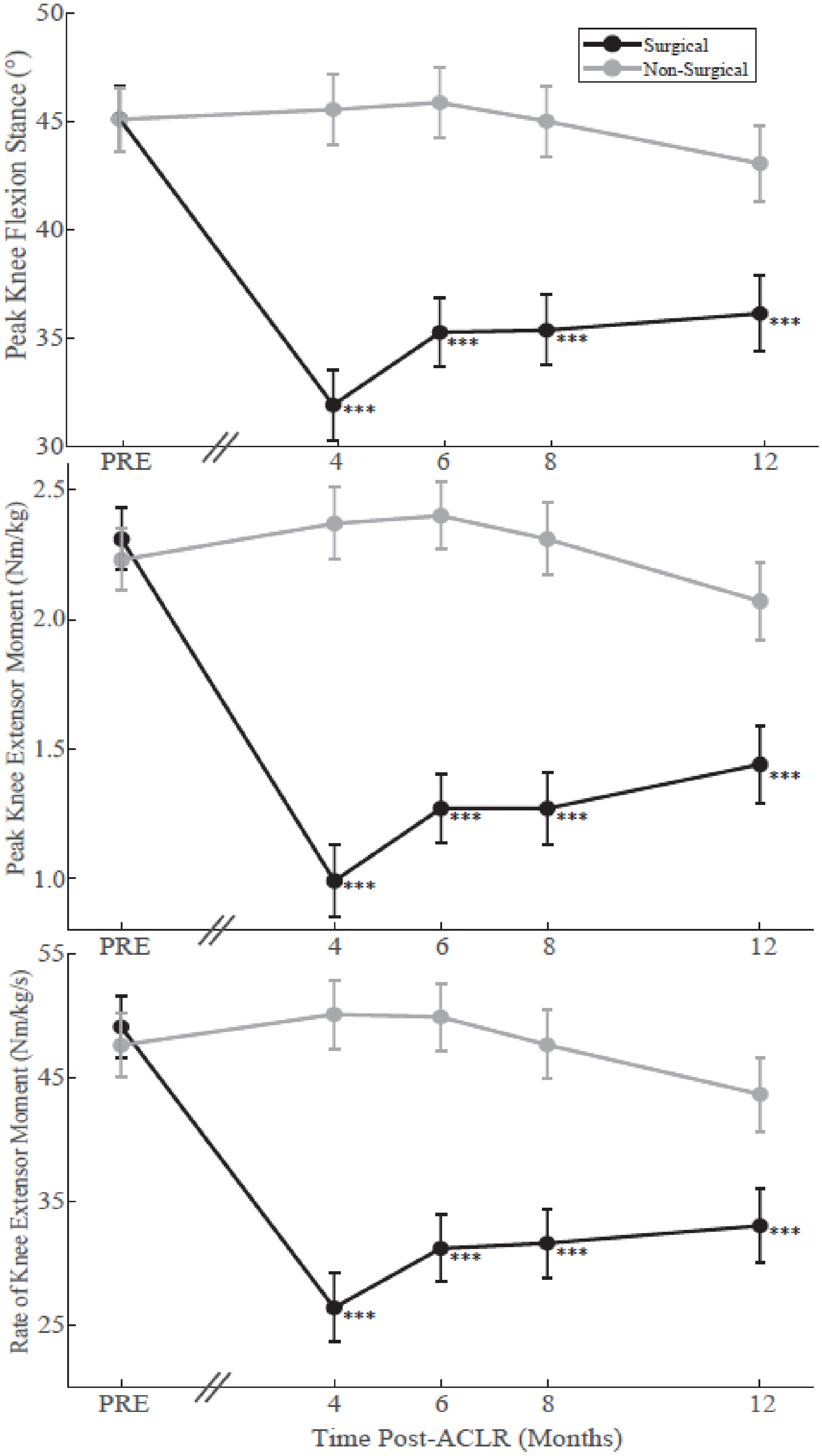

Surgical
Non-Surgical
Peak Knee Flexion Stance (°)
50
45
40
35
30
***
Peak Knee Extensor Moment (Nm/kg)
2.5
2.0
1.5
1.0
Rate of Knee Extensor Moment (Nm/kg/s)
55
45
35
25
PRE
4
6
8
12
Time Post-ACLR (Months)

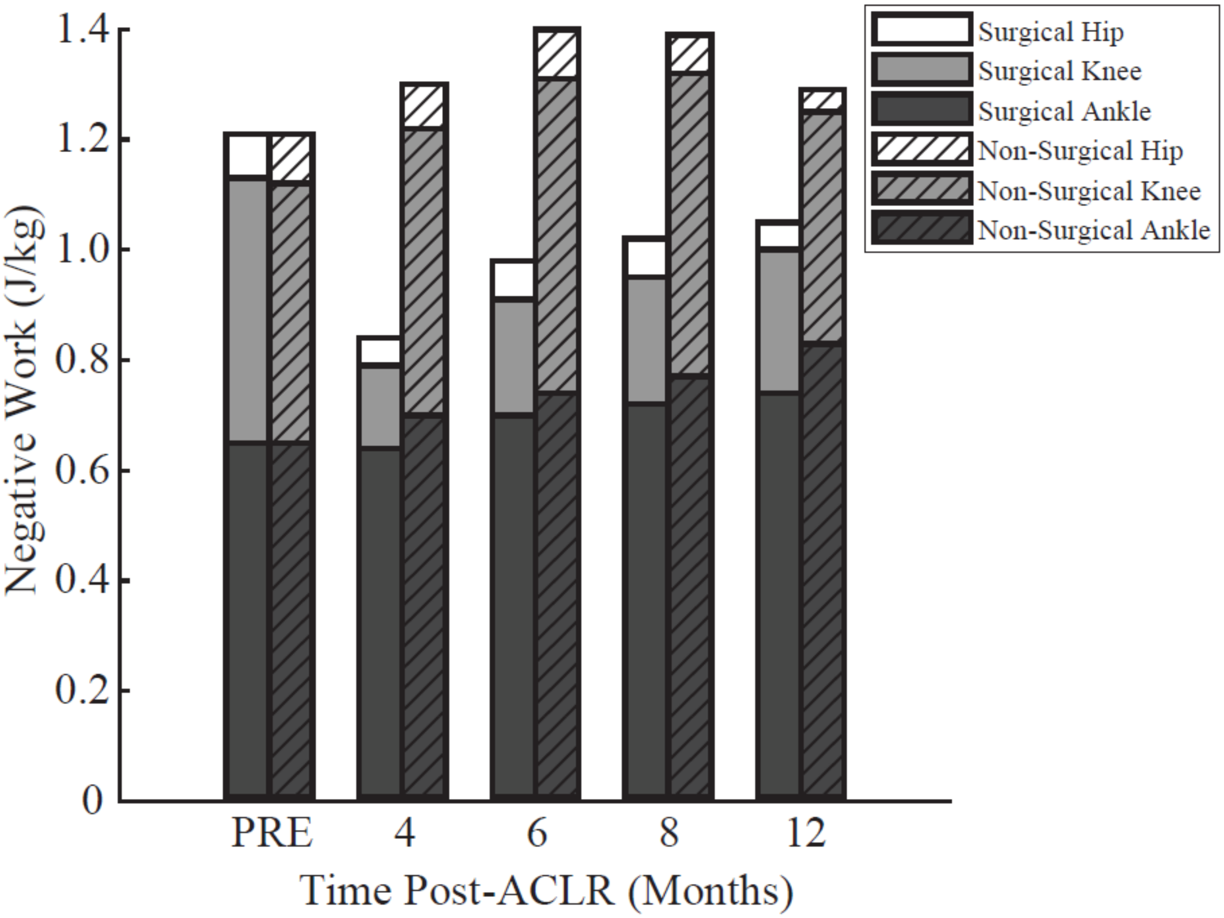
Table 1.2. Least-square means, standard errors (SE), mean differences from pre-injury, and Tukey-adjusted p-values for surgical and non-surgical limb running biomechanical variables of interest at all time-points. A negative value notes a deficit in the post-operative collection compared to pre-injury.

Biomechanical Variable	**Limb**	**Pre-Injury**	**4-Months**			**6-Months**		
		Mean (SE)	Mean (SE)	Mean Difference from Pre-Injury (% Change)	p-value	Mean (SE)	Mean Difference from Pre-Injury (% Change)	p-value
Vertical Ground Reaction Force Impulse (Ns/kg)	Surgical	3.58 (0.07)	3.27 (0.07)	-0.31 (-8.7%)	<0.001	3.34 (0.07)	-0.24 (-6.7%)	<0.001
	Non-Surgical	3.54 (0.07)	3.65 (0.07)	0.11 (3.1%)	0.22	3.66 (0.07)	0.12 (3.4%)	0.13
Braking Ground Reaction Force Impulse (Ns/kg)	Surgical	0.21 (0.007)	0.17 (0.008)	-0.04 (-19.0%)	<0.001	0.18 (0.008)	-0.03 (-14.3%)	<0.001
	Non-Surgical	0.21 (0.007)	0.24 (0.008)	0.03 (14.3%)	<0.001	0.25 (0.008)	0.04 (19.0%)	<0.001
Peak Knee Flexion Angle During Stance (°)	Surgical	45.2 (1.5)	32.0 (1.6)	-13.2 (-29.2%)	<0.001	35.3 (1.6)	-9.9 (-21.9%)	<0.001
	Non-Surgical	45.1 (1.5)	45.6 (1.6)	0.5 (1.1%)	0.99	45.9 (1.6)	0.8 (1.8%)	0.99
Peak Knee Extensor Moment (Nm/kg)	Surgical	2.31 (0.12)	0.99 (0.14)	-1.32 (-57.1%)	<0.001	1.27 (0.13)	-1.04 (-45.0%)	<0.001
	Non-Surgical	2.23 (0.12)	2.37 (0.14)	0.14 (6.3%)	0.98	2.40 (0.13)	0.17 (7.6%)	0.94
Rate of Knee Extensor Moment (Nm/kg/s)	Surgical	49.10 (2.52)	26.42 (2.76)	-22.68 (-46.2%)	<0.001	31.21 (2.70)	-17.89 (-36.4%)	<0.001
	Non-Surgical	47.61 (2.52)	50.10 (2.76)	2.49 (5.2%)	0.99	49.89 (2.70)	2.28 (4.8%)	0.99

Biomechanical Variable	**Limb**	**Pre-Injury**	**8-Months**			**12-Months**		
		Mean (SE)	Mean (SE)	Mean Difference from Pre-Injury (% Change)	p-value	Mean (SE)	Mean Difference from Pre-Injury (% Change)	p-value
Vertical Ground Reaction Force Impulse (Ns/kg)	Surgical	3.58 (0.07)	3.45 (0.07)	-0.13 (-3.6%)	0.13	3.46 (0.08)	-0.12 (-3.4%)	0.36
	Non-Surgical	3.54 (0.07)	3.69 (0.07)	0.15 (4.2%)	0.04	3.57 (0.07)	0.03 (0.8%)	0.99
Braking Ground Reaction Force Impulse (Ns/kg)	Surgical	0.21 (0.007)	0.19 (0.008)	-0.02 (-9.5%)	0.01	0.20 (0.008)	-0.01 (-4.8%)	0.87
	Non-Surgical	0.21 (0.007)	0.25 (0.008)	0.04 (19.0%)	<0.001	0.24 (0.008)	0.03 (14.3%)	0.004

Peak Knee Flexion Angle During Stance (°)	Surgical	45.2 (1.5)	35.4 (1.6)	-9.8 (-21.7%)	<0.001	36.2 (1.74)	-9.0 (-19.9%)	<0.001
	Non-Surgical	45.1 (1.5)	45.0 (1.6)	-0.1 (-0.2%)	0.99	43.1 (1.7)	-2.0 (-4.4%)	0.94
Peak Knee Extensor Moment (Nm/kg)	Surgical	2.31 (0.12)	1.27 (0.14)	-1.04 (-45.0%)	<0.001	1.44 (0.15)	-0.87 (-37.7%)	<0.001
	Non-Surgical	2.23 (0.12)	2.31 (0.14)	0.08 (3.6%)	0.99	2.07 (0.15)	-0.16 (-7.2%)	0.98
Rate of Knee Extensor Moment (Nm/kg/s)	Surgical	49.10 (2.52)	31.63 (2.77)	-17.47 (-35.6%)	<0.001	33.04 (2.97)	-16.06 (-32.7%)	<0.001
	Non-Surgical	47.61 (2.52)	47.64 (2.77)	0.03 (0.1%)	0.99	43.65 (2.97)	-3.96 (-8.3%)	0.88

Figure 1.3. Negative work performed by the hip, knee and ankle of each limb during the stance phase of running at each time point. Knee negative work of the surgical limb was significantly (all p-values <0.001) reduced at all post-anterior cruciate ligament reconstruction (ACLR) time-points relative to pre-injury (PRE). Solid filled bars depict the surgical limb, while diagonal slash filled bars depict the non-surgical limb.



A significant time*limb interaction was detected for total negative work (p-value < 0.001), but not for hip or ankle negative work (p values>0.71). Total negative work was significantly reduced within the surgical limb at 4 (-0.37±0.06 J/kg, p<0.001) and 6 months (-0.23±0.06 J/kg, p=0.01), but not at 8 (-0.18±0.06 J/kg, p=0.12) or 12 months (-0.15±0.07 J/kg, p=0.38) (Figure

1.3). A time main effect was observed for ankle negative work averaged across both limbs demonstrating an increase at 12 months only (0.13±0.07 J/kg, p=0.01) compared to pre-injury. Within the non-surgical limb, no significant differences in total negative work were detected at any time-point compared to pre-injury (all p-values>0.07) (Figure 1.3).

A significant time*limb interaction was detected for vertical GRF impulse and braking impulse (p-values<0.001). The surgical limb demonstrated significant reductions in vertical GRF impulse at 4 and 6 months (both p<0.001) and braking impulse at 4, 6, and 8 months (all p-values<0.01). In contrast, the non-surgical limb demonstrated a significant increase in vertical GRF impulse at 8 months (p=0.04) and braking impulse at all time-points (all p-values<0.004; table 1.2).

Discussion

The purpose of this study was to assess bilateral changes in running biomechanics from pre-injury throughout the first year post-ACLR in NCAA Division I collegiate athletes. Significant alterations were observed, with most metrics not returning to pre-injury values by 12 months post-ACLR on the surgical limb. These data partially supported our primary hypothesis that GRFs and knee joint kinematics and kinetics of the surgical limb during running would not return to pre-injury levels by 12-months following ACLR. This pattern was observed for knee kinematics and kinetics; however, surgical limb vertical GRF and braking impulses were significantly reduced shortly after ACLR, but restored to within pre-injury levels by 6 and 8 months, respectively. Our secondary hypothesis was also partially supported as non-surgical limb GRF impulses were significantly altered, but knee kinematics and kinetics did not change significantly from the pre-injury assessment.

This is the first study, to the authors' knowledge, to longitudinally quantify changes in running biomechanics throughout the first year post-ACLR compared to pre-injury. Within the surgical limb, significant reductions in peak knee flexion angle, peak knee extensor moment, rate of knee extensor moment, and knee negative work were observed at all time-points compared to the pre-injury values. Previous cross-sectional studies observed significant deficits compared to the non-surgical limb in peak knee flexion angle (pooled mean difference -2.72° [95% confidence interval (CI): -4.45,-0.99]) and stance phase peak knee extensor moment (pooled standardized mean difference -0.62 [95% CI: -0.87,-0.36]) between 3 months and 5 years following ACLR.[92] While not directly comparable as we assessed differences from pre-injury, our results demonstrate a greater magnitude of deficit in the surgical limb, with knee flexion deficits during stance ranging from -13.2° to -9.0° and standardized mean difference of peak knee extensor moment during stance ranging from -3.09 to -2.07 throughout the first 12 months post-ACLR (Figure 1.2). This discrepancy in the magnitude of change within the surgical limb between our study and the systematic review of cross-sectional studies may be due, in part, to the majority of studies included in the review reporting data greater than 12 months post-operative. As our study is the first to assess bilateral changes in running mechanics within the first year post-ACLR compared to the pre-injury state, an appropriate comparison dataset does not exist. In a cohort of healthy collegiate athletes, normative between limb asymmetries were 2.2° ± 0.2 for peak knee flexion angle, 9.7±1.0% for peak knee extensor moment, and 15.8±1.5% for knee negative work.[134] In the current study, we observed surgical limb deficits at 12-months post-ACLR of 9.0° for peak knee flexion angle, 37.7% for peak knee extensor moment, and 45.8% for knee negative work, which are well outside of these normative ranges. Despite not reporting between-limb asymmetries, comparing our findings to this healthy cohort may provide greater clinical context to the magnitude of deficits observed in our sample. Regardless of the differences in magnitude found in prior studies and the present work, it is evident that surgical limb knee mechanics during running remain significantly altered beyond a time when most athletes return to sport and have completed post-operative rehabilitation. It remains unknown if these altered movement patterns are adopted as a protective mechanism in an attempt to reduce joint stresses or if they may simply be the result of impaired neuromuscular performance.

Our unique dataset provides novel insights into whether the non-surgical limb is an appropriate comparator for the surgical limb. In short, the knee joint metrics of the non-surgical limb were consistent over time compared to the pre-injury state, which may support the use of the non-surgical limb as a comparator for knee-specific biomechanics throughout the rehabilitation process. This particular finding has important clinical implications as most sports medicine facilities utilize the non-surgical limb as a reference when assessing return-to-sport readiness and generally do not have pre-injury data as a comparator. Further studies with larger sample sizes will be needed to corroborate these findings.

Conversely, substantial alterations in GRFs of the non-surgical limb were detected. Braking impulse within the non-surgical limb was increased by 14.3% to 19.0% at all time-points post-ACLR compared to pre-injury, while the surgical limb demonstrated a 19.0% to 9.5% decrease at 4 and 8 months, respectively. Additionally, the non-surgical limb demonstrated a significant increase (4.2%) in vertical GRF impulse at 8 months, while the surgical limb decreased 8.7% and 6.7% at 4 and 6 months, respectively, compared to pre-injury. As such, utilizing the contralateral limb as a reference of recovery for these particular variables will likely conflate the true deficits when compared to using pre-injury as a reference. Moreover, recovery of running biomechanics post-ACLR should not be based solely on GRF variables, as these returned to pre-injury levels within the surgical limb earlier than knee specific kinematics and kinetics. Finally, the greater GRFs observed on the non-surgical limb may increase that limb’s injury risk to a running-related injury, and warrants further investigation.

We also sought to determine the distribution of negative work performed by the joints of the surgical and non-surgical limbs to assess for compensatory movement strategies, as biomechanical and neuromuscular compensations have been observed during walking, running, squatting, and jumping following ACLR.[9,51,89,129,131] The underlying cause of these observed compensations may be due, in part, to persistent joint pain,[126] impaired quadriceps performance,[51,56,93,131,133] reduced joint proprioception,[109] or lack of confidence following ACLR.[96,115,139] We found significant reductions in total negative work in the surgical limb at 4 and 6 months (p-values<0.01). The significant reduction in knee negative work at all time-points (all p-values<0.002) and the lack of time*limb interaction for hip and ankle negative work suggests that the knee is the primary contributor to the change in the surgical limb's total negative work (Figure 1.3). Within the non-surgical limb, a statistically significant change from the pre-injury state was not detected for total negative work, but a potential increase in total negative work post-operatively was observed (p-values = 0.07 and 0.16 at 6 and 8 months, respectively) (Figure 1.3).

By 3 to 4 months post-surgery the majority of the athletes in our study initiated running. This is consistent with prior research indicating that most athletes resume running ~3 months following ACLR.[106] This time period coincides with when the knee mechanics displayed the greatest deficit from pre-injury. Initiating running with such significant gait abnormalities may lead athletes to adopt compensatory movement patterns that are detrimental to long-term joint health.[3,17,132] Abnormal quadriceps function is likely a primary contributor to the substantial running deficits observed at the 4- and 6-month time-points. Indeed, deficits in quadriceps neuromuscular performance and strength are nearly universal early after ACLR[58,105] and have been associated with reduced knee flexion angles and extensor moments during hopping[93] and walking[133], as well as rate of knee extensor moment during running.[95] Further, subtle changes in quadriceps force production, neuromuscular coordination, and associated movement kinematics can significantly increase knee cartilage loads during activities including walking and running.[11,56,57,130,150] The altered running biomechanics we observed throughout the initial year post-ACLR likely have a significant effect on tibiofemoral[10,123] and patellofemoral cartilage loading.[10,39,132] However, previous studies in this area are of cross-sectional design, which limits our understanding of how knee cartilage loading changes over time. Understanding longitudinal changes in knee cartilage loading is an important next step in this line of research, as altered knee joint loading has been suggested to contribute to early onset osteoarthritis.[3,17,132]

This is the first study to our knowledge to assess changes in running biomechanics in elite collegiate athletes. As the athletes in this study were highly trained prior to sustaining an ACL injury, results may not generalize to other age groups or levels of competition. Despite frequent and unrestricted access to sports medicine facilities and resources, substantial biomechanical deficits were observed in this cohort. In a general sports medicine population with more restricted access to post-surgical care, the magnitude of the observed running alterations may be even more pronounced. Although not all athletes underwent testing at every time-point, we used linear mixed effects models to account for missing data within subjects. Additionally, all athletes had bone-patellar tendon-bone grafts, limiting the potential generalizability to other graft types. Due to the small sample size of this study, the observed effects may be inflated. The sample size also limited our ability to investigate the effects of potential confounders such as sex and concomitant surgical procedures (e.g. meniscus repair). However, the results from this study support the need for future healthy baseline screening and development of larger datasets to assess for the potential influence of these confounders.

In conclusion, substantial reductions in knee flexion angle, extensor moment, and negative work during running were evident in the surgical limb throughout the first 12 months post-ACLR, when compared to pre-injury. Additionally, the non-surgical limb appears to be a valid reference of recovery for the surgical knee-specific running mechanics following ACLR, but not for GRF variables.

Chapter 2. Effect of Running Speed on Knee Biomechanics in Collegiate Athletes Following Anterior Cruciate Ligament Reconstruction

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(Note: this chapter is prepared for submission to Medicine and Science in Sports and Exercise)

Abstract

Purpose: During running, athletes post-anterior cruciate ligament reconstruction (ACLR) demonstrate altered surgical knee kinematics and kinetics compared to the non-surgical limb and healthy controls. The effect of running speed on biomechanics has not been formally assessed in athletes post-ACLR. The purpose of this study was to characterize how knee biomechanics change with running speed between 4-7 and 8-12 months post-ACLR.

Methods: Fifty-six Division I collegiate athletes post-ACLR completed running analyses (4-7 months: n=41, 8-12 months: n=42, both: n=27) at 2.68, 2.95, 3.35, 3.80 and 4.47 m/s. Linear mixed effects models assessed the influence of limb, speed, time post-ACLR, and their interactions on ground reaction forces, knee kinematics, and knee kinetics.

Results: A significant limb*speed interaction was detected for peak knee flexion and rate of knee extensor moment (p-values <0.02), controlling for time. From 3.35 to 4.47 m/s, peak knee flexion increased 0.5° (95% CI: -0.6, 1.5°) in the non-surgical limb and 1.8° (95% CI: 0.7, 2.9°) in the surgical limb. Peak vertical ground reaction force, peak knee extensor moment, and knee negative work increased similarly with speed for both limbs (p-values < 0.002). A significant limb*time interaction was detected for all variables (p-values < 0.001). Accounting for running speed, improvements in all surgical limb biomechanics were observed from 4-7 to 8-12 months (p-values < 0.001), yet between-limb differences remained (p-values < 0.001).

Conclusion: Surgical and non-surgical knee biomechanics increase similarly with speed in collegiate athletes at both 4-7 and 8-12 months post-ACLR, with the exception of peak knee

flexion and rate of knee extensor moment. Surgical knee biomechanics improved from 4-7 and 8-12 months post-ACLR, but significant between-limb differences persisted.

Introduction

Following anterior cruciate ligament reconstruction (ACLR), altered running biomechanics are typically observed and commonly include reduced knee flexion angles and knee extensor moments of the surgical limb.[92] These altered mechanics are most pronounced early post-operatively and improve throughout rehabilitation, yet still persist beyond the typical return to sport time frame.[54,87] Not only are these altered knee mechanics a concern for an athlete's performance and re-injury risk upon returning to sport, but they may play a key role in the onset and progression of post-traumatic knee osteoarthritis.[17] As such, there is a need to identify strategies that mitigate the altered knee loading during running that is commonly observed post-ACLR.

Resuming running is a key milestone for athletes as part of ACLR rehabilitation. Typically, athletes are recommended to resume running at a slow speed (2.22–2.78 m/s) around 12 weeks post-operatively, with few studies reporting performance based-criteria for this recommendation.[106] The recommendation to resume running at a slow speed is based on expert opinion,[106] as the effect of modulating running speed on biomechanics post-ACLR has yet to be formally studied. In healthy athletes, an incremental increase in running speed corresponds to an increase in knee flexion angles and knee extensor moments,[30,90] but has no effect on between-limb asymmetries.[134] As underloading of the surgical knee during running is a typical alteration observed post-ACLR, increasing speed may be a viable treatment option to elicit greater knee extensor demand during running. Further, understanding how time post-operatively influences the effect of running speed on knee biomechanics will inform when running speed may be most important to consider. As quadriceps neuromuscular performance is more impaired early post-operatively,[141] athletes may not possess the adequate quadriceps torque generating capacity necessary to respond to an increase in running speed. Therefore, they may adopt a maladaptive movement strategy to run at a faster speed. Better understanding the influence of speed and time post-ACLR on running mechanics may assist rehabilitation specialists in tailoring interventions in an attempt to mitigate compensatory movement strategies.

The purpose of this study was to characterize how knee biomechanics change with running speed in NCAA Division I Collegiate athletes post-ACLR at two clinically relevant time points (between 4-7 months and 8-12 months). We hypothesized that with an increase in speed surgical knee kinematics and kinetics during running would increase more in the non-surgical limb compared to the surgical limb between 4-7 months post-ACLR, and that both limbs would increase similarly between 8-12 months post-ACLR.

Methods

Participants

This study analyzed routinely collected running data from the Badger Athletic Performance database (November 2011-December 2022). The database contains longitudinal results from standardized post-ACLR testing, including running, of Division I collegiate athletes at the University of Wisconsin-Madison. An athlete's records were extracted if they met the following criteria: 1) underwent a primary ACLR, 2) had no lower extremity surgery within 12 months before the primary ACLR, 3) had a running analysis performed between 4-7 months and/or 8-12 months post-ACLR, and 4) had data for at least 2 running speeds at the included time point. This records review was approved by the university's Health Sciences Institutional Review Board.

Running Analysis

As part of the standard post-operative testing protocol, athletes ran on an instrumented treadmill (Bertec Corporation, Columbus, OH), while marker-based, three-dimensional motion analysis was concurrently performed. First, 52 reflective markers (23 on anatomical landmarks) were placed on the athlete. Then, a static standing posture was recorded, which was later used to identify hip joint centers and for model scaling. To acclimate to the treadmill, athletes initially walked for 2 minutes and then ran at multiple speeds. Speed was incrementally increased from 2.68 m/s to 4.47 m/s (10 min/mile to 6 min/mile, at 1 min/mile increments) or until the athlete reached their self-reported maximum comfortable speed. Kinematics and ground reaction forces (GRF) were recorded for 15 s at each speed. Kinematics were sampled at 200 Hz using an 8-camera system (Motion Analysis Corporation, Santa Rosa, CA) and recorded synchronously with GRF, which were sampled at 2000 Hz.

Inverse kinematic and dynamic routines were performed as previously described.[38] A 14-segment, 31 degrees-of-freedom articular linkage, scaled to the athlete's height, mass, and segment lengths, was used to model the body. Kinematic and GRF data were low-pass filtered using a bi-directional, 4th-order Butterworth filter with a cutoff frequency of 12 Hz, which were both used for the segment-by-segment inverse dynamics analysis to calculate joint moments. Separately, GRF data were low-pass filtered using a bi-directional, 4th-order Butterworth filter with a cutoff frequency of 50 Hz. These data were used for stance phase identification using a 50 N threshold for vertical GRF.[135] Variables of interest included: peak knee flexion angle, peak vertical GRF, peak knee extensor moment, rate of knee extensor moment (slope from 20-80% of peak knee extensor moment), and knee negative work (area under the negative knee power curve during loading response). Multiple knee kinetic variables were selected as each may provide complimentary but distinct information about how an athletes is running.[136] All signal and data processing was conducted using MATLAB (Release 2018b; MathWorks, Inc).

Statistical Analysis

Standard descriptive statistics (mean and standard deviation or frequency and percentage, as appropriate) were used to describe the athlete sample. Multivariable linear mixed effects models assessed the influence of speed, limb, and time post-ACLR on biomechanics during running. All three- and two-way interactions were assessed for significance and retained in the model if significant. Speed (5 levels), limb (2 levels), and time (2 levels) were treated as categorical variables. Athlete and limb were assigned as random effects (limb nested within athlete). Tukey-adjusted P-values were used for all pairwise comparisons. Least square means and associated 95% confidence intervals [lower bound, upper bound] are reported. A sensitivity analysis was performed for peak knee extensor moment and peak knee flexion models to determine the influence of including athletes that did not achieve faster running speeds (e.g. only ran at 2.68 and 2.95 m/s). The least square mean values from the complete dataset were compared to a reduced dataset that only included athletes that achieved at least 3.80 m/s. Statistical analyses were performed using R (version 4.1.3; R Core Team), and significance was assessed at $\alpha = 0.05$.

Results

The records review criteria identified 56 Division I collegiate athletes for inclusion (41 athletes between 4-7 months; 42 athletes between 8-12 months; Figure 2.1). Athlete demographics are reported in Table 2.1 and are separated by time point post-ACLR. Twenty-seven athletes had running analyses at both time points. No 3-way interactions between limb, time post-operatively, and speed were detected for any variable (all p-values > 0.52). Parameter estimates for the interaction and main effects of each model are provided in Table 2.2.

Figure 2.1. Records extraction process. ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction.

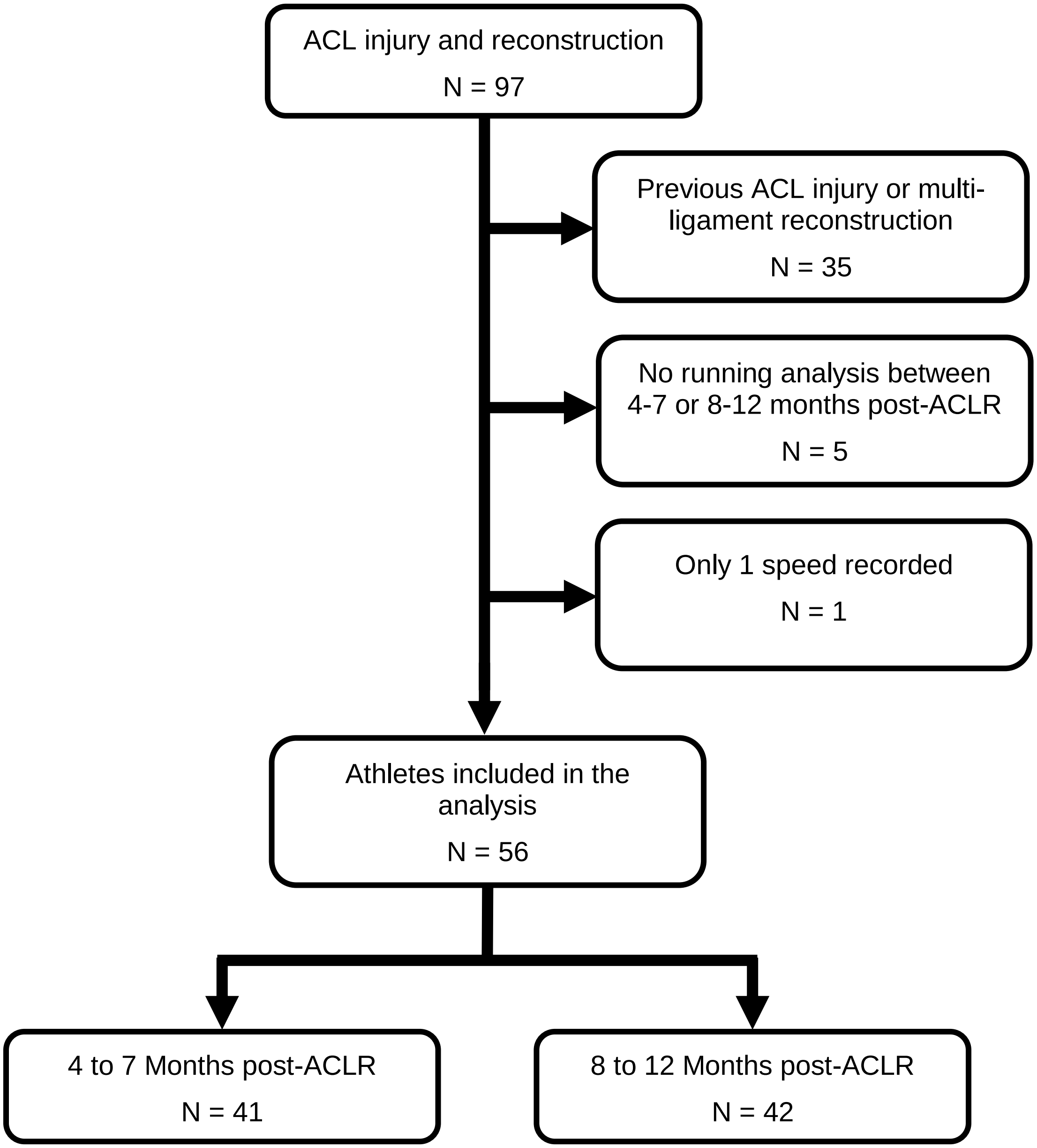


Table 2.1. Summary of athlete demographics. Values are presented as mean (SD) unless otherwise indicated. MPFL, medial patellofemoral ligament

	4 to 7 Months Post-ACLR	8 to 12 Months Post-ACLR	Overall
N	41	42	56
Age, y	21.0 (1.4)	21.0 (1.5)	21.0 (1.4)
Body Mass, kg	86.1 (18.1)	81.6 (16.4)	84.9 (17.0)
Height, m	1.80 (0.10)	1.78 (0.10)	1.79 (0.10)
Body Mass Index, kg/m^2	26.5 (4.2)	25.6 (3.2)	26.3 (3.8)
Females, n (%)	15 (36.6)	20 (47.6)	24 (42.9)
Graft type, n (%)			
Bone-patellar-tendon-bone	34 (82.9)	36 (85.7)	46 (82.1)
Hamstring tendon	1 (2.4)	3 (7.1)	3 (5.4)
Quadriceps tendon	6 (14.6)	3 (7.1)	7 (12.5)
Concomitant procedures, n (%)			
Meniscectomy	11 (26.8)	10 (23.8)	15 (26.8)
Meniscal repair	12 (29.3)	9 (21.4)	15 (26.8)
MPFL reconstruction	1 (2.4)	1 (2.4)	1 (1.8)
Time post-operatively, months	5.5 (1.0)	9.9 (1.6)	
Observations at each speed, n (%)			
2.68 m/s	39 (24.4)	42 (23.9)	
2.95 m/s	38 (23.8)	37 (21.0)	
3.35 m/s	39 (24.4)	40 (22.7)	
3.80 m/s	27 (16.9)	31 (17.6)	
4.47 m/s	17 (10.6)	26 (14.8)	

Table 2.2. Fixed effect estimates, including all significant 2-way interactions, from linear mixed effects models assessing the influence of time post-anterior cruciate ligament reconstruction, limb, and speed on knee biomechanics during running. The non-surgical limb is the reference for the main effect of limb. The 4-7 months post-operative group is the reference for the main effect of time. The 2.68 m/s collection is the reference for the main effect of speed. CI, confidence interval; *, 2-way interaction.

	peak knee flexion (°)		**peak vertical ground reaction force (N/kg)**		**peak knee extensor moment (Nm/kg)**		**rate of knee extensor moment (Nm/kg/s)**		**knee negative work (J/kg)**	
Model Fixed Effects:	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**
(Intercept)	44.1 (42.7, 45.5)	<0.001	22.7 (22.1, 23.2)	<0.001	2.09 (1.97, 2.22)	<0.001	37.9 (35.7, 40.2)	<0.001	0.47 (0.43, 0.51)	<0.001
Limb	-11.6 (-12.8, -10.4)	<0.001	-1.7 (-2.0, -1.4)	<0.001	-1.13 (-1.24, -1.02)	<0.001	-15.8 (-18.1, -13.5)	<0.001	-0.34 (-0.37, -0.31)	<0.001
Time	-0.7 (-1.2, -0.3)	0.002	0.4 (0.2, 0.6)	<0.001	-0.04 (-0.09, 0.00)	0.053	-0.6 (-1.5, 0.3)	0.174	-0.02 (-0.03, -0.01)	0.004
Speed (2.95 m/s)	0.6 (0.1, 1.2)	0.027	1.0 (0.9, 1.2)	<0.001	0.09 (0.06, 0.13)	<0.001	3.8 (2.7, 4.9)	<0.001	0.02 (0.01, 0.03)	0.002
Speed (3.35 m/s)	1.2 (0.7, 1.8)	<0.001	2.0 (1.8, 2.1)	<0.001	0.19 (0.16, 0.23)	<0.001	8.6 (7.5, 9.7)	<0.001	0.04 (0.03, 0.05)	<0.001
Speed (3.80 m/s)	1.5 (0.9, 2.1)	<0.001	2.8 (2.6, 2.9)	<0.001	0.29 (0.25, 0.33)	<0.001	13.3 (12.1, 14.5)	<0.001	0.06 (0.05, 0.08)	<0.001
Speed (4.47 m/s)	1.7 (1.0, 2.3)	<0.001	3.7 (3.5, 3.9)	<0.001	0.37 (0.33, 0.42)	<0.001	18.3 (17.0, 19.6)	<0.001	0.07 (0.06, 0.08)	<0.001
Limb * Time	3.8 (3.2, 4.5)	<0.001	1.0 (0.7, 1.2)	<0.001	0.39 (0.33, 0.45)	<0.001	6.3 (5.1, 7.6)	<0.001	0.12 (0.10, 0.14)	<0.001
Limb * Speed (2.95 m/s)	0.4 (-0.4, 1.2)	0.316					-1.0 (-2.6, 0.5)	0.197		

Limb * Speed (3.35 m/s)	0.8 (0.1, 1.6)	0.037					-2.1 (-3.6, -0.6)	0.008		
Limb * Speed (3.80 m/s)	1.4 (0.6, 2.3)	0.001					-2.6 (-4.3, -0.9)	0.003		
Limb * Speed (4.47 m/s)	2.1 (1.2, 3.1)	<0.001					-1.7 (-3.6, 0.1)	0.071		

Effect of Speed

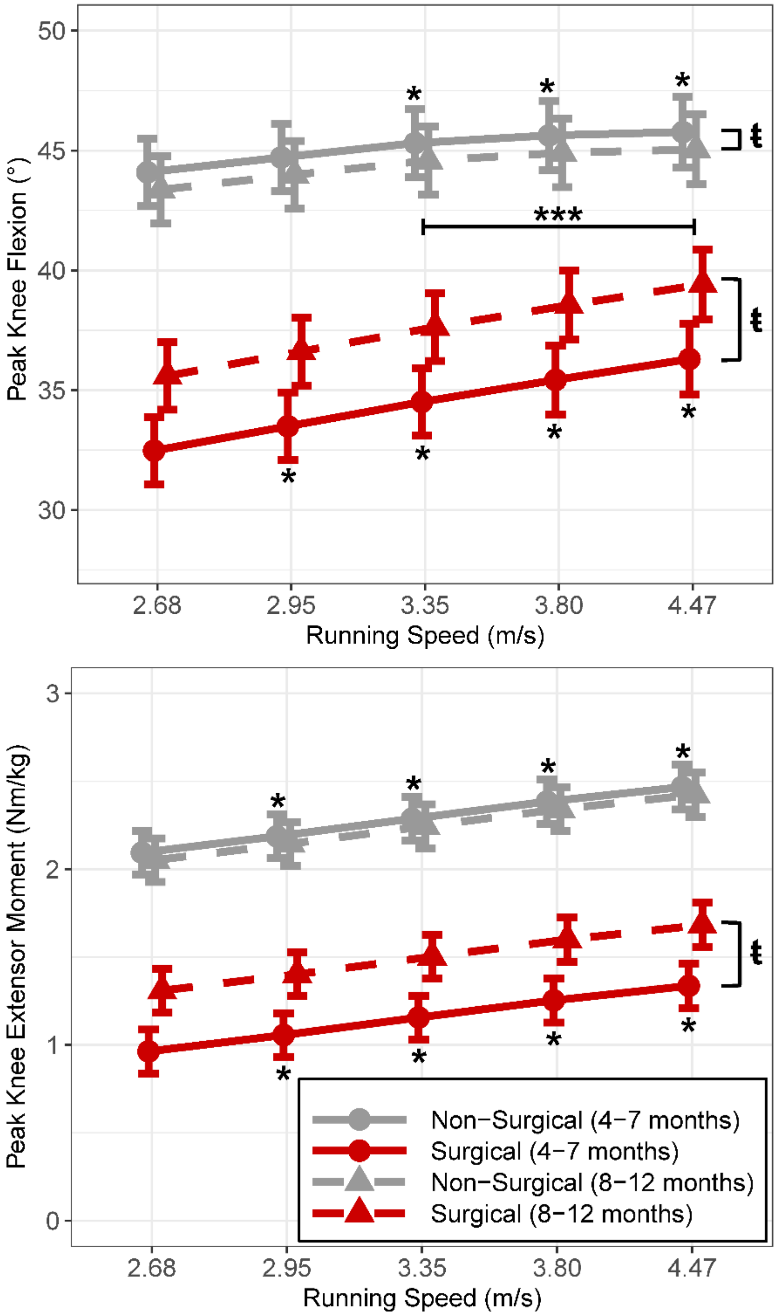
For peak vertical ground reaction force (p-value = 0.93), peak knee extensor moment (p-value = 0.44), and knee negative work (p-value = 0.38), no significant interaction between limb and speed was detected. Peak vertical ground reaction force, peak knee extensor moment (Figure 2.2), and knee negative work demonstrated a linear increase similarly across limbs, when accounting for time post-operatively. All speed main effects can be found in Table 2.2.

For peak knee flexion angle (p-value < 0.001) and rate of knee extensor moment (p-value = 0.02), a significant interaction between limb and speed was detected. The increase in peak knee flexion angle was greater for the surgical limb than the non-surgical limb from 3.35 to 4.47 m/s (Figure 2.2). For rate of knee extensor moment, when accounting for time, the non-surgical limb increased significantly between 3.35 to 3.80 m/s (4.72 Nm/kg/s [2.78, 6.66], p-value < 0.001) and between 3.80 and 4.47 m/s (4.97 Nm/kg/s [2.72, 7.21], p-value < 0.001). The surgical limb increased between 3.35 to 3.80 m/s (4.21 Nm/kg/s [2.27, 6.15], p-value < 0.001) and between 3.80 and 4.47 m/s (5.82 Nm/kg/s [3.55, 8.09], p-value < 0.001).

Effect of Time Post-ACLR

A significant interaction between limb and time post-operatively was detected for all variables (all p-values <0.001). We observed an increase in peak vertical ground reaction force in both limbs from 4-7 to 8-12 months post-ACLR, with a greater magnitude of change in the surgical limb (1.36 N/kg [1.12, 1.59], p-value < 0.001) compared to the non-surgical limb (0.40 N/kg [0.17, 0.63], p-value < 0.001), when accounting for speed. For peak knee extensor moment, when accounting for speed, no difference between time points was identified in the non-surgical limb (-0.04 Nm/kg [-0.10, 0.01], p-value = 0.21). However, the surgical limb increased between time points (0.35 Nm/kg [0.29, 0.40], p-value < 0.001) (Figure 2.2; Supplemental File 2.1, Appendix 1). For knee negative work, when accounting for speed, we observed a reduction in the non-surgical limb (-0.02 J/kg [-0.04, -0.002], p-value = 0.02) between time points, while the surgical limb increased (0.10 J/kg [0.08, 0.11], p-value < 0.001).

Figure 2.2. Least square means and 95% confidence intervals for peak knee flexion angle (top) and peak knee extensor moment (bottom) across running speeds for both limbs and time points. *, significant within-limb difference from 2.68 m/s (Tukey-adjusted p-values < 0.01) when accounting for time; ***, significant interaction between limb and speed (p-value < 0.001); ŧ, significant within-limb change over time (Tukey-adjusted p-values < 0.009) when accounting for speed.



Sensitivity Analysis

The sensitivity analysis demonstrated minimal differences in peak knee flexion (range = 0.1 to 0.7°) and peak knee extensor moment (range = 0.02 to 0.07 Nm/kg) when comparing the full dataset to the reduced dataset with only athletes that achieved 3.80 m/s (Supplemental File 2.1, Appendix 1).

Discussion

This study aimed to describe the effect of running speed on knee biomechanics in collegiate athletes post-ACLR between two clinically relevant time points. Contrary to our primary hypothesis, peak vertical ground reaction force, peak knee extensor moment, and knee negative work all increased similarly to the non-surgical limb with running speed, irrespective of time post-operatively. A similar relationship for peak knee flexion angle and rate of knee extensor moment was observed, although we found some slight differences between limbs at the faster speeds. Consistent with our secondary hypothesis, surgical knee mechanics improved irrespective of running speed from 4-7 to 8-12 months post-ACLR for all variables of interest.

This is the first study to our knowledge that directly assesses the relationship between running speed and knee biomechanics following ACLR. Similar to previous studies with healthy athletes [30,90], increased running speed corresponded with an increase in peak knee flexion angles and knee kinetics in athletes following ACLR. These speed-related increases were consistent across both the surgical and non-surgical limbs, with the exception of peak knee flexion and rate of knee extensor moment. From 3.35 to 4.47 m/s, peak knee flexion increased, on average, only 0.5° in the non-surgical limb, while the surgical limb increased 1.8°, on average. Although these differences are relatively small with questionable clinical utility, the results suggest that increasing running speed may improve between limb asymmetries in peak knee flexion angle. At the very least, the findings from this study demonstrate that increasing running speed (from 2.68 to 4.47 m/s) in athletes following ACLR does not increase between-limb differences in knee biomechanics.

As the speed-related changes in peak vertical ground reaction force, peak knee extensor moment, and knee negative work did not differ between limbs (no speed-by-limb interaction was detected), the between limb differences remained significant across all speeds. Therefore, the percent increase from the slowest speed (2.68 m/s) was greater for the surgical limb than the non-surgical limb. For example, the least square mean values for peak knee extensor moment at 4-7 month post-ACLR of the surgical limb were 0.96 and 1.34 Nm/kg at 2.68 and 4.47 m/s, respectively, while the non-surgical limb values were 2.09 and 2.47 Nm/kg at 2.68 and 4.47 m/s, respectively (Figure 2.2). Although the increases in peak knee extensor moment from 2.68 to 4.47 m/s were the same for both limbs (0.38 Nm/kg), the change relative to the slowest speed equates to a 28.4% increase in the surgical limb and only a 15.4% increase in the non-surgical limb. Therefore, the perceived demand on the knee extensors during running may be greater on the surgical limb than the non-surgical limb with an increase in speed.

Another interesting observation is the influence that running speed has on limb symmetry indices (LSIs), $(Surgical \div Non - Surgical) \times 100,$ of knee biomechanics during running. Although not directly assessed in this study, we can estimate LSIs for knee biomechanics from the least square mean values, which may provide better clinical context as LSIs are commonly used in a clinical setting.[12,14] Using the same least square mean values for peak knee extensor moment from the previous paragraph, the LSI at 2.68 m/s is 45.9%, while the LSI at 4.47 m/s is 54.3%. The change in peak knee extensor moment LSI with speed is simply due to an increase in magnitude of both limbs (0.38 Nm/kg) and does not reflect greater recovery of the surgical limb as one may intuitively interpret an increased LSI. Therefore, speed is an important factor to consider when assessing LSIs of knee biomechanics during running.

Contrary to our initial hypothesis, we did not detect a difference in the effect of speed on knee biomechanics during running between the early (4-7 months) and late (8-12 months) time points post-operatively. This hypothesis was based off of the premise that surgical limb quadriceps neuromuscular performance (e.g. knee extensor torque and rate of torque development) is substantially impaired early post-operatively and typically improves throughout the rehabilitation process.[20,45,52,58,137] As such, athletes 4-7 months post-ACLR may not be able to rapidly generate the knee extensor torques necessary to respond to an increase in running speed. However, athletes were assessed at submaximal running speeds (for short durations). In general, running, particularly at the speeds assessed in this study, does not require maximal quadriceps recruitment,[31,80,95,124] and therefore, the ability to generate maximal rate or magnitude of knee extensor torque may not be a limiting factor. The primary difference between time points was that the surgical limb demonstrated a significant improvement in all knee biomechanics variables assessed. Despite this improvement, significant deficits remained between limbs for all variables at the later time point. These results are consistent with our previous findings in which collegiate athletes demonstrated significant surgical limb deficits in knee biomechanics during running at 4-months post-ACLR, that improved out to 12-months, yet remained significantly less than preinjury and non-surgical limb levels.[54] These persistent deficits do not seem to simply resolve with time, as abnormal running mechanics have been observed 5 and 8 years post-ACLR.[32,87] These findings are concerning as altered sagittal plane knee kinematics and kinetics likely lead to asymmetrical cartilage loading,[123,132] which has been suggested as a mechanism for post-traumatic knee osteoarthritis.[17] As such, future work is needed to identify other factors or interventions to mitigate these knee loading deficiencies during running.

Although this study provides novel insight into the effects of speed on running biomechanics following ACLR, some important limitations should be considered. This study consists of routinely collected clinical data. As a result, not all athletes completed testing at both time points and not all athletes ran at all speeds. Linear mixed effects models were utilized to help account for athletes with only one time point, and a sensitivity analysis demonstrated no significant difference in the dataset used for this study versus a reduced dataset of only athletes that obtained 3.80 m/s. Further, running speed was incrementally increased and not randomized. The lack of randomization may influence the findings; however, an incremental protocol was chosen to ensure athlete safety and provide a gradual warm up in preparation for faster speeds. Although it appears that increasing running speed has a positive effect on knee biomechanics, clinicians should use caution when applying these findings to practice as we did not assess the direct effect on cartilage or self-reported pain. Rehabilitation was completed in the same facility, under similar post-operative rehabilitation protocols, but was not controlled between athletes. As the data for this study came from Division I collegiate athletes post-ACLR, most with bone-patellar-tendon bone grafts, findings may not generalize to other ages, competition levels, and graft types.

In conclusion, as running speed increases, knee kinematics and kinetics increase similarly in both the surgical and non-surgical limbs of collegiate athletes post-ACLR, with the exception of peak knee flexion and rate of knee extensor moment, which demonstrate subtle variations between limbs at faster running speed (3.35 to 4.47 m/s). Time post-ACLR does not influence the effect of speed on knee biomechanics. Irrespective of speed, surgical knee biomechanics improved from 4-7 to 8-12 months post-ACLR, but significant between-limb differences remained.

Chapter 3. Quadriceps Rate of Torque Development has Greater Influence than Strength on Recovery of Knee Biomechanics during Running after Anterior Cruciate Ligament Reconstruction

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(Note: this chapter is currently under review at the American Journal of Sports Medicine)

Abstract

Background: After anterior cruciate ligament-reconstruction (ACLR), altered surgical knee biomechanics during running is common. While better quadriceps strength is associated with better running knee kinetic symmetry post-ACLR, abnormal running mechanics persist even after resolution of quadriceps strength deficits. As running is a submaximal effort task characterized by limited time to develop knee extensor torque, quadriceps rate of torque development (RTD) may have a greater impact on recovery of running knee mechanics than peak torque (PT).

Hypothesis/Purpose: To assess the influence of recovery in quadriceps PT and RTD symmetry on knee kinematic and kinetic symmetry during running over the initial 2-years post-ACLR.

Study Design: Cohort study; Level of evidence, 2.

Methods: Following ACLR, 39 Division I collegiate athletes (106 observations, 19 females) completed serial isometric performance testing and running analyses between 3 and 24 months. Athletes performed maximal and rapid isometric knee extension efforts with each limb to assess PT and RTD between-limb symmetry indices (PT_{LSI}, RTD_{LSI}), respectively. Peak knee flexion difference (PKF_{DIFF}) and peak knee extensor moment LSI ($PKEM_{LSI}$) during running were computed. Multivariable linear mixed effects models assessed the influence of PT_{LSI} and RTD_{LSI} on PKF_{DIFF} and $PKEM_{LSI}$ over the initial 2 years post-ACLR.

Results: Significant main effects of RTD_{LSI} (p-values < 0.001) and time (p-values ≤ 0.02) but not PT_{LSI} (p-values ≥ 0.24) were observed for both PKF_{DIFF} and $PKEM_{LSI}$ models. For a 10% increase in RTD_{LSI}, while controlling for PT_{LSI} and time, a 0.9° (95% CI: 0.5°, 1.3°) reduction in PKF_{DIFF} and a 3.5% (95% CI: 1.9%, 5.1%) increase in $PKEM_{LSI}$ are expected. For every month post-ACLR, a 0.2° (95% CI: 0.05°, 0.38°) reduction in PKF_{DIFF} and a 1.3% (95% CI: 0.6%, 2.0%) increase in $PKEM_{LSI}$ are expected, controlling for PT_{LSI} and RTD_{LSI}.

Conclusion: Quadriceps RTD_{LSI} is more strongly associated with symmetrical knee biomechanics during running compared to PT_{LSI} or time throughout the first 2-years post-ACLR.

Clinical Relevance: Longitudinally assessing RTD in addition to PT post-ACLR provides a more comprehensive understanding of quadriceps muscle capacity and may better correlate with movement biomechanics. Interventions to restore quadriceps RTD_{LSI} should be emphasized in post-surgical rehabilitation.

Key Words: ACL, Running, Biomechanics, general, Collegiate Athlete, Quadriceps Strength, Rate of Torque Development

Introduction

After anterior cruciate ligament-reconstruction (ACLR), significant alterations in running biomechanics are common.[92] These changes are most apparent in the surgical limb where reduced knee flexion angles and extensor moments are typically present, with minimal changes in the non-surgical limb.[54,92] Unfortunately, this between-limb asymmetry does not seem to resolve simply with time, as deficits have been observed out to 5 years post-ACLR.[87] Persistent alterations in movement mechanics can lead to impaired performance,[86,151] increased risk of future injury,[49,61] and cartilage degeneration.[3,17,99] Asymmetrical movement mechanics coincide with altered knee cartilage loading of the surgical limb, which may contribute to the sequela of osteoarthritis (OA) following ACLR.[3,17] As such, restoring symmetrical knee loading, particularly during a repetitive task such as running, is likely an important step in reducing the onset and progression of OA in this population.

Restoring quadriceps strength is a primary focus of rehabilitation following ACLR and assessment of peak knee extensor torque production is commonly included in return to sport testing batteries.[2] Better quadriceps strength, i.e., greater peak knee extensor torque, has been associated with improved knee mechanics during walking,[63,101,128] running,[7,63] and jump landing[72] and better knee cartilage health.[99,100,103] Despite these findings, abnormal knee mechanics during gait persist even after resolution of quadriceps strength deficits,[5,116] suggesting that using quadriceps strength assessment as a proxy for movement symmetry is inadequate. This is not surprising considering the time needed to produce maximal knee extensor torque is 500 ms or greater.[138] Typical daily and athletic tasks are characterized by short bursts of muscle activation (50-200 ms).[16,31,107] As such, quadriceps rate of torque development (RTD) may have a greater impact than quadriceps strength on the recovery of knee mechanics during running.[51]

Despite the theoretical influence of quadriceps RTD on movement biomechanics, current empirical evidence is limited. In athletes following ACLR, better quadriceps RTD has generally been found to be weakly associated with better self-reported knee function,[22,40] walking ground reaction forces,[140] vertical and crossover hop performance,[64,105] and running and jumping kinetics.[41,95] However, most of these studies have been limited to cross-sectional designs with relatively small samples, and often with subjects who are years removed from surgery, which may confound the influence RTD has on movement biomechanics. As the majority of athletes return to sport at or before 1 year post-surgery, a longitudinal cohort beginning earlier post-surgery is needed to determine the influence quadriceps strength and RTD have on restoration of running mechanics in athletes following ACLR. In highly competitive athletes, restoration of quadriceps RTD following ACLR may be an important differentiator of those that are able to return to sport and compete at their prior level of performance.

The purpose of this study was to assess the influence of recovery in quadriceps strength and RTD symmetry on knee flexion angle and extensor moment symmetry during running over the initial 2-years post-ACLR in NCAA Division I collegiate athletes. We hypothesized that recovery of RTD symmetry would have the strongest association with recovery of knee biomechanics symmetry during running.

Methods

Participants

Data for this study were identified via records review of the Badger Athletic Performance database between January 2017 and July 2022. This database contains routinely collected performance and healthcare data from Division I collegiate athletes at the University of Wisconsin-Madison. Data of interest included serial quadriceps isometric performance and running biomechanics testing. An athlete's records were extracted if they met the following criteria: 1) underwent a primary ACLR, 2) had no lower extremity surgery within 12 months before the primary ACLR, 3) had both quadriceps isometric performance testing and running analysis within 1 week of each other, and 4) testing was completed between 3 and 24 months post-ACLR. If an athlete sustained a second ACL injury or underwent another lower extremity surgery within the 24-month period post-ACLR, only data prior to this injury/surgery were included. This records review was approved by the university's Health Sciences Institutional Review Board.

Running Assessment and Analysis

Marker-based, three-dimensional motion analysis was performed while athletes ran on an instrumented treadmill (Bertec Corporation, Columbus, OH). A standard protocol was utilized as previously described.[135] Athletes walked for 2 minutes and then ran with speed incrementally increased from 2.68 m/s to 4.47 m/s (10 min/mile to 6 min/mile) or until the athlete reached their self-reported maximum comfortable speed. In total, 52 reflective markers (23 on anatomical landmarks) were placed on each athlete.[38] To identify hip joint centers and for model scaling, a static standing posture was recorded. Kinematics were sampled at 200 Hz using an 8-camera system (Motion Analysis Corporation, Santa Rosa, CA) and recorded synchronously with ground reaction forces (GRF), which were sampled at 2000 Hz. Kinematics and GRF were recorded for 15 seconds at each speed. The maximum comfortable speed, consistent across all collections within an athlete, was used for subsequent analyses.

Inverse kinematic and dynamic routines were performed as previously described.[38] GRF and kinematic data were low-pass filtered using a bi-directional, 4th-order Butterworth filter with a cutoff frequency of 12 Hz. A 14-segment articular linkage, scaled to the athlete's height, mass, and segment lengths, was used to model the body. To identify the stance phase of running, a 50 N threshold for vertical GRF was used.[135] Peak knee extensor moment (PKEM) normalized to body mass and peak knee flexion angle (PKF) during the stance phase were averaged across 15 strides for both limbs. A limb symmetry index (LSI) was calculated for PKEM

(PKEM$_{\mathrm{LSI}}$) and defined as: $(Surgical\ Limb \div Non\text{-}Surgical\ Limb) \times 100$. To characterize the asymmetry in PKF (PKF$_{\mathrm{DIFF}}$), the between limb difference was calculated as the surgical limb PKF angle minus the non-surgical PKF angle. Therefore, a negative value for PKF$_{\mathrm{DIFF}}$ represents reduced PKF on the surgical limb compared to the non-surgical limb. PKEM$_{\mathrm{LSI}}$ and PKF$_{\mathrm{DIFF}}$ were both used in the statistical analyses.

Isometric Quadriceps Performance Assessment and Analysis

Athletes performed isometric quadriceps performance testing on an electromechanical dynamometer with the knee positioned at 90° and hip positioned at 85° (Biodex System 4, Biodex Medical Systems, Shirley, NY). The knee adapter pad was positioned 5 cm proximal to the medial malleolus and in the reverse orientation to reduce compliance.[73] The non-surgical limb was always tested first. Athletes performed a progressive warmup at 50%, 75%, and 90% of maximum effort, which was followed by two 5-second maximal voluntary isometric knee extension contractions (MVIC). Loud verbal encouragement and visual feedback of the torque signal were provided. MVIC trials were repeated if greater than a 10% difference was observed between trials.

After MVIC efforts were completed on a given limb, athletes performed rapid voluntary isometric contractions in the same position. They were instructed to kick as fast and as hard as possible.[119] A progressive warmup, with repetitions at 50%, 75%, 90%, and 100% of maximum effort, was completed prior to a minimum of five maximal effort recorded repetitions. Trials were initiated by an auditory signal and continued until torque production plateaued for 2-3 seconds. If a countermovement in the torque signal occurred prior to the rise in torque, the repetition was discarded and another was completed.[118]

For all isometric efforts, torque signals were sampled at 2000 Hz. All torque signals were rectified, low-pass filtered using a bi-directional 3rd-order Butterworth filter with a cutoff frequency of 60 Hz, and baseline offsets were removed. The global peak knee extensor torque

(PT) across two MVIC trials was identified. For the rapid effort trials, the rate of torque development (RTD) was calculated as the slope of the torque signal from 20% to 80% of peak torque.[23] The best three of five recorded trials for each limb were averaged to maximize between-session reliability.[35] PT and RTD LSIs (PT_{LSI} and RTD_{LSI}) were calculated as: $(Surgical\ Limb \div Non\text{-}Surgical\ Limb) \times 100$. All data processing was performed using a custom Matlab script (Release 2018b, Mathworks, Inc., Natick, MA).

Statistical Analyses

Standard descriptive statistics (mean and standard deviation or frequency and percentage, as appropriate) were used to describe the athlete population. Multivariable linear mixed effects models were used to assess the influence of PT_{LSI}, RTD_{LSI}, and time post-ACLR on PKF_{DIFF} and $PKEM_{LSI}$ during running following ACLR. Athlete and time post-ACLR were assigned as random effects. All two-way interactions were assessed for significance and retained if significant. Model estimates and 95% confidence intervals are provided as well as each model's total variance explained by the fixed effects (marginal R^2) and each independent variable's variance explained (partial R^2).[85] Statistical analyses were performed using R (version 4.1.3; R Core Team).

Results

Following the records review process, 39 Division I collegiate athletes (106 observations between 3 and 24 months post-ACLR) were identified for inclusion (Figure 3.1). Athlete demographics are reported in Table 3.1. The number of observations for a given athlete ranged from 1 to 7, with a median of 3 [interquartile range: 1, 4]. The distribution of observations over time post-ACLR can be found in Supplemental Table 3.1 (Appendix 2). The average running speed across all athletes was 3.9 ± 0.6 m/s.

Figure 3.1. Records extraction process. All athletes included in the analysis had both isometric quadriceps performance testing and running biomechanics analyses on or within 1 week of each other post-anterior cruciate ligament reconstruction. ACL, anterior cruciate ligament.

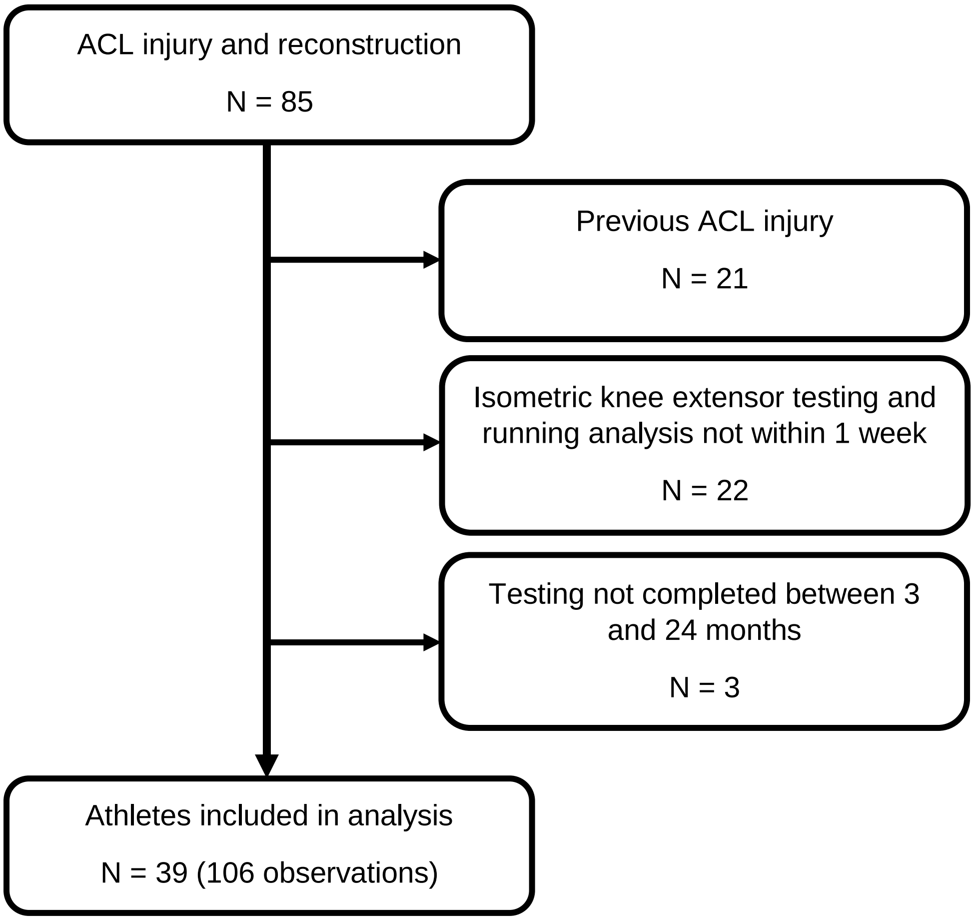


Table 3.1. Athlete demographics

Participant Information (N = 39)	
	Values
Total Observations	106
Age, y[a]	20.4 (1.5)
Body Mass, kg[a]	82.7 (19.2)
Height, m[a]	1.78 (0.09)
Body Mass Index, kg/m^2[a]	26.0 (4.7)
Females, n (% of total participants)	19 (47.5)
Graft type, n (% of total participants)	
Bone-patellar-tendon-bone	32 (82)
Hamstring tendon	4 (10)
Quadriceps tendon	3 (8)
Concomitant procedures, n (% of total participants)	
Meniscectomy	8 (21)
Meniscal repair	10 (26)
Medial Patellofemoral Ligament reconstruction	2 (5)
Time post-operatively, months[c]	10.1 (5.5)
Range	3.1, 24.9
Knee Biomechanics during Running[c]	
Surgical limb peak flexion, °	38.2 (6.4)
Between-limb difference, °[b]	-7.9 (5.2)
Surgical limb peak extensor moment, Nm/kg	1.48 (0.56)
Limb symmetry index, %	62.7 (22.4)
Isometric Quadriceps Performance Values[c]	
Surgical limb peak torque, Nm/kg	2.68 (0.80)
Limb symmetry index, %	78.3 (19.7)
Surgical limb rate of torque development, Nm/kg/s	7.81 (3.57)
Limb symmetry index, %	59.7 (25.5)

[a], Based on first post-operative assessment; [b], A negative between limb difference represents reduced knee flexion on the surgical limb; [c], Based on all observations.

Running Peak Knee Flexion Difference

No significant two-way interactions were detected for the PKF_{DIFF} model (PT_{LSI} * RTD_{LSI}, p = 0.68; PT_{LSI} * time, p = 0.89; RTD_{LSI} * time, p = 0.54). The total variance explained by the fixed effects was $R^2 = 0.48$. A significant main effect of RTD_{LSI} was observed ($p < 0.001$), but not PT_{LSI} (p = 0.24, Table 3.2). For a 10% increase in RTD_{LSI}, a 0.9° (95% CI: 0.5°, 1.3°) reduction in PKF_{DIFF} is expected, on average, adjusting for time post-ACLR and PT_{LSI} (Figure 3.2). A significant main effect of time post-ACLR was observed (p = 0.02, Table 3.2). For every month post-ACLR, a 0.2° (95% CI: 0.1°, 0.4°) reduction in PKF_{DIFF} is expected, on average, adjusting for RTD_{LSI} and PT_{LSI} (Figure 3.2). When PT_{LSI} was the only quadriceps performance variable included in the model the effect of PT_{LSI} was significant ($p < 0.001$), but the models total variance explained was reduced compared to the full model ($R^2 = 0.42$, Supplemental Table 3.2). Conversely, when RTD_{LSI} was the only quadriceps performance variable included in the model the effect of RTD_{LSI} remained significant ($p < 0.001$), and the models total variance explained was retained compared to the full model ($R^2 = 0.48$, Supplemental Table 3.3, appendix 2).

Running Peak Knee Extensor Moment LSI

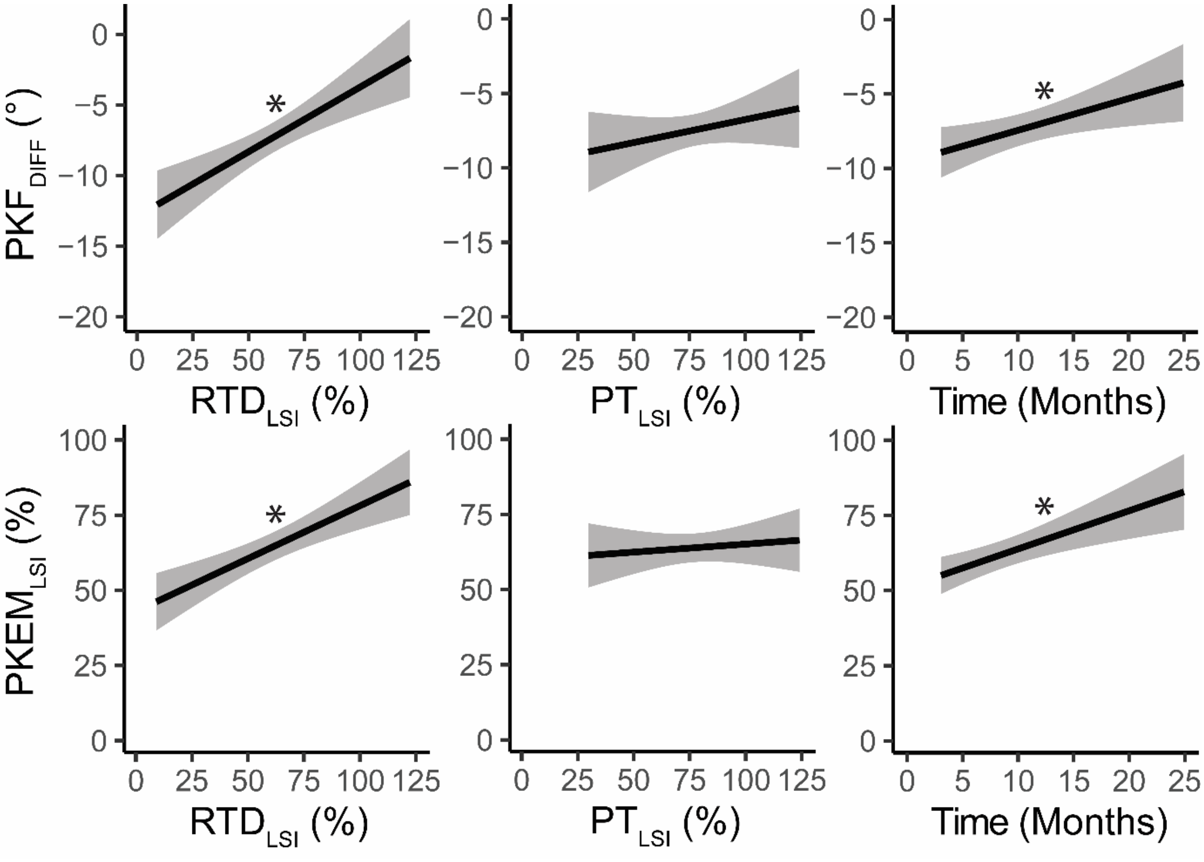
No significant two-way interactions were detected for the $PKEM_{LSI}$ model (PT_{LSI} * RTD_{LSI}, p = 0.23; PT_{LSI} * time, p = 0.68; RTD_{LSI} * time, p = 0.21). The total variance explained by the fixed effects was $R^2 = 0.53$. A significant main effect of RTD_{LSI} was observed ($p < 0.001$), but not for PT_{LSI} (p = 0.60, Table 3.2). For a 10% increase in RTD_{LSI}, a 3.5% (95% CI: 1.9%, 5.1%) increase in $PKEM_{LSI}$ is expected, on average, adjusting for time post-ACLR and PT_{LSI} (Figure 3.2). A significant main effect of time post-ACLR was observed (p = 0.001, Table 3.2). For every month post-ACLR, a 1.3% (95% CI: 0.6%, 2.0%) increase in $PKEM_{LSI}$ is expected, on average, adjusting for RTD_{LSI} and PT_{LSI} (Figure 3.2). When PT_{LSI} was the only quadriceps performance variable included in the model the effect of PT_{LSI} was significant (p = 0.001), but the model's total variance explained was reduced compared to the full model ($R^2 = 0.36$, Supplemental Table 3.2). Conversely, when RTD_{LSI} was the only quadriceps performance variable included in the model the effect of RTD_{LSI} remained significant ($p < 0.001$), and the model's total variance explained was minimally reduced compared to the full model ($R^2 = 0.47$, Supplemental Table 3.3, appendix 2).

Table 3.2. Linear mixed effects models for the effect of time post-anterior cruciate ligament reconstruction (Time), knee extensor peak torque limb symmetry index (PT_{LSI}), rate of torque development limb symmetry index (RTD_{LSI}) on peak knee flexion difference (PKF_{DIFF}) and peak knee extensor moment limb symmetry index ($PKEM_{LSI}$). A negative PKF_{DIFF} represents reduced knee flexion on the surgical limb.

		Estimate (95% CI)	p-value	Partial R^2 (95% CI)
PKF_{DIFF} (°)	(Intercept)	-17.49 (-20.33, -14.65)	<0.001	
	PT_{LSI} (%)	0.03 (-0.03, 0.08)	0.24	0.009 (0.00, 0.08)
	RTD_{LSI} (%)	0.09 (0.05, 0.13)	<0.001	0.13 (0.04, 0.26)
	Time (months)	0.21 (0.05, 0.38)	0.02	0.05 (0.00, 0.16)
$PKEM_{LSI}$ (%)	(Intercept)	25.96 (15.71, 36.21)	<0.001	
	PT_{LSI} (%)	0.05 (-0.14, 0.25)	0.60	0.002 (0.00, 0.05)
	RTD_{LSI} (%)	0.35 (0.19, 0.51)	<0.001	0.11 (0.02, 0.23)
	Time (months)	1.27 (0.56, 1.98)	0.001	0.09 (0.02, 0.22)

CI, confidence interval

Figure 3.2 The modeled relationships of each independent variable with peak knee flexion difference (PKF_{DIFF}) (top row) and peak knee extensor moment limb symmetry index ($PKEM_{LSI}$) (bottom row) during running post-anterior cruciate ligament reconstruction (ACLR) when adjusting for all other independent variables. The black lines are the estimated linear relationship with 95% confidence interval in grey. A negative PKF_{DIFF} represents reduced knee flexion on the surgical limb. ***** = independent variable had a significant main effect ($p<0.05$). Rate of torque development limb symmetry index, RTD_{LSI}; Knee extensor peak torque limb symmetry index, PT_{LSI}; Months post-ACLR, Time.



Discussion

The purpose of this study was to assess the influence of recovery in quadriceps PT and RTD symmetry on knee flexion angle and extensor torque symmetry during the stance phase of running over the initial 2-years post-ACLR in NCAA Division I collegiate athletes. Consistent with our hypothesis, quadriceps RTD_{LSI} was more strongly associated with the recovery of knee biomechanics symmetry during running than PT_{LSI}. Additionally, when adjusting for PT_{LSI} and RTD_{LSI}, time post-ACLR was also significantly associated with the recovery of knee biomechanics during running.

This is the first study to longitudinally assess the influence that both PT and RTD have on running biomechanics over the initial 2 years post-ACLR. We detected stronger associations between RTD and movement mechanics than previous studies.[41,64,95] Possible explanations for this discrepancy include variations in the methods used to calculate RTD (e.g. RTD 20-80% vs 0-100ms from onset), time frames assessed post-operatively, the task performed (e.g. running vs single leg hop for distance), and/or the biomechanical variables of interest. One exception is a prospective study that assessed the relationships between quadriceps RTD and hop performance at 3 and 6 months post-ACLR and found a similar variance explained ($R^2 \sim 0.4$) when both RTD and PT were included in the model.[105]

PT and RTD provide insight into two different constructs of quadriceps performance. PT is a measurement of the ability to generate maximal knee extensor torque irrespective of time. RTD is a measure of quadriceps performance that characterizes the ability to produce knee extensor torque rapidly.[73] During running, the knee extensors are constrained in their ability to generate torque to the time the foot is on the ground (~150-300 ms),[16,31] and therefore athletes are unable to utilize the maximum torque capacity of the knee extensors.[138] This may explain why RTD_{LSI} is more strongly associated with the recovery of knee mechanics during running compared to PT_{LSI}. An inability to rapidly produce knee extensor torque may lead to compensatory movement strategies during running that are typically characterized by PKEM and PKF deficits of the surgical knee.[92] Therefore, restoring RTD_{LSI} may be a prerequisite to re-establishing symmetrical running mechanics post-ACLR.

Although we did not detect an association between PT_{LSI} and knee biomechanics asymmetry during running when controlling for RTD_{LSI} and time post-ACLR, PT remains an important characterization of quadriceps muscle function post-ACLR. In fact, when only time and PT_{LSI} were included in the $PKEM_{LSI}$ model, PT_{LSI} had a significant effect and explained 36% of the variance in $PKEM_{LSI}$, albeit to a lesser extent than RTD_{LSI} ($R^2 = 0.47$). The relationships between quadriceps strength and post-ACLR outcomes have been thoroughly investigated, with better quadriceps strength associated with reduced re-injury risk,[34] more symmetrical movement mechanics,[72] and better patient-reported outcomes scores.[102] PT and RTD represent unique but correlated aspects of muscle function. The ability to generate large knee extensor torques rapidly (RTD) is predicated on the ability to generate large knee extensor torques, independent of time (PT). Significant quadriceps weakness results in both reduced PT and RTD, and is thus a limiting factor to restoring knee biomechanics symmetry during running.

Differentiating PT and RTD becomes more important clinically as PT_{LSI} improves.[13] An athlete with satisfactory PT_{LSI} and RTD_{LSI} may be well positioned for returning to running post-ACLR, but an athlete with sufficient PT_{LSI} but poor RTD_{LSI} may lack the rapid quadriceps torque generating capacity necessary to run without compensatory strategies. As our data suggests, the latter situation may be relatively common following ACLR, with the athletes in this study achieving an average of >78% PT_{LSI}, but <60% RTD_{LSI} post-ACLR.

Quadriceps strength testing following ACLR is common clinical practice and is recommended by ACL clinical practice guidelines.[2,66,78] Knee extensor RTD is more challenging to assess than PT in a clinical setting, as it requires a rigid system, low signal-to-noise ratio, and a high sampling rate.[73] In addition, while strength is almost universally quantified via PT, there are many options for characterizing RTD (e.g. as the peak slope, from contraction onset within a specified interval, or the time to reach a specified torque output), with no consensus on the most clinically relevant method.[73] Therefore, RTD assessments are rarely incorporated into clinical decision making and are not included in current clinical practice guidelines. Future work should determine what RTD variables and/or methods are most clinically meaningful and develop protocols for clinically feasible assessment of quadriceps RTD with patients post-ACLR.

It is important to note that 52% and 47% of the variance in the PKF_{DIFF} and $PKEM_{LSI}$ models, respectively, remains unexplained by the variables assessed in this study. Other clinical factors need to be considered such as pain, effusion, psychological state, and timing of when an athlete begins to run post-ACLR. Initiating running post-ACLR without adequate quadriceps torque generating capacity may lead athletes to adopt maladaptive movement strategies to perform the task. As running is a repetitive and routine movement pattern for athletes, this maladaptive movement strategy may become ingrained and persist long-term post-ACLR.[87] Unfortunately, these altered movement strategies likely have a negative effect on long-term joint health.[3,17] Running retraining strategies aimed at reducing PKF_{DIFF} and improving $PKEM_{LSI}$ may be necessary once an adequate level of quadriceps performance is achieved.

As the data from this study come from a clinical database, not every athlete had the same number of observations and the time in which observations occurred varied between athletes. In addition, fewer observations occurred beyond 12 months, which is reflected in the wider 95% confidence intervals, particularly at 24 months. To account for variation in the timing of athlete observations and missing data, linear mixed-effects models were used. Rehabilitation was not controlled in this study; however, athletes completed their rehab in the same sports medicine facility under similar post-operative rehabilitation protocols and had unrestricted access to sports medicine facilities and resources. All athletes in this study were Division I collegiate athletes and the majority had a bone-patellar-tendon bone graft, which may limit the generalizability of findings to other ages, competition levels, and graft types.

Quadriceps RTD_{LSI} was more strongly associated with the recovery of knee biomechanics symmetry during running than PT_{LSI} throughout the first 2-years post-ACLR. Quadriceps RTD_{LSI}, PT_{LSI}, and time post-ACLR accounted for 48% of the variance in PKF_{DIFF} and 53% of the variance in $PKEM_{LSI}$. Restoring not just quadriceps maximal strength but rapid torque production is important post-ACLR to facilitate recovery of knee biomechanics symmetry during running.

Chapter 4. Quadriceps Performance and Running Biomechanics Influence Femur BMD Changes After ACL Reconstruction in Collegiate Athletes

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(Note: this chapter is currently under review at the Medicine and Science in Sports and Exercise)

Abstract

Purpose: Reduced bone mineral density of the distal femur (BMD_{DF}) can persist long-term following anterior cruciate ligament reconstruction (ACLR), even in athletes who return to high levels of competition. These deficits may have implications for the onset and progression of knee osteoarthritis. It is unknown if clinically modifiable factors are associated with losses in BMD_{DF}. This study evaluated the potential influence of knee extensor peak torque (PT), rate of torque development (RTD), as well as peak knee flexion angle (PKF) and peak knee extensor moment (PKEM) during running, on longitudinal changes in BMD_{DF} post-ACLR.

Methods: Following ACLR, 57 Division I collegiate athletes underwent serial whole-body DXA scans between 3 and 24 months post-ACLR. Of these, 43 athletes also had isometric knee extensor testing (21 female, 105 observations) and 54 had running analyses (26 female, 141 observations). Linear mixed effects models, controlling for sex, assessed the influence of surgical limb quadriceps performance (PT and RTD), running mechanics (PKF and PKEM), and time post-ACLR on BMD_{DF} (5% and 15% of femur length). Simple slope analyses were used to explore interactions.

Results: Athletes with RTD below 7.20 Nm/kg/s (mean) at 9.3 months post-ACLR demonstrated significant decreases in 15% BMD_{DF} over time ($p = .03$). Athletes with PKEM during running below 0.92 Nm/kg (-1 SD below mean) at 9.8 months post-ACLR demonstrated significant decreases in 15% BMD_{DF} over time (p = .02). Significant slopes were not detected at -1 SD below the mean for PT (1.75 Nm/kg, p = .07) and PKF (31.3°, p = .08).

Conclusion: Worse quadriceps RTD and running PKEM were associated with a greater loss of BMD_{DF} between 3 and 24 months post-ACLR.

Key Terms: Bone, Knee, Biomechanics, Running, Isometric, RTD

Introduction

Persistent reductions in surgical limb bone mineral density (BMD) of the proximal tibia and distal femur has been observed following anterior cruciate ligament reconstruction (ACLR).[46,88] It has been speculated that limited weight bearing, joint disuse, and immobilization post-ACLR all contribute to BMD loss over time.[88] BMD deficits seem to be most pronounced about the surgical knee.[77,82,112] Even in National Collegiate Athletic Association (NCAA) Division I athletes who return to high levels of competition, distal femur BMD deficits persisted at 2 years post-operatively.[53] It remains unknown what neuromuscular factors are associated with these long-term BMD changes.

One factor that may contribute to femur BMD deficits is quadriceps muscle weakness, which is commonly observed post-ACLR.[65] Quadriceps performance assessments (e.g. peak torque and rate of torque development) are commonly used to quantify the magnitude of quadriceps impairment and guide clinical decision making following ACLR.[66] Quadriceps weakness is associated with poor functional outcomes,[43] increased risk of secondary ACL injury,[34] and may contribute to the early onset of osteoarthritis (OA) that is common in this population.[94] Despite quadriceps strengthening being a focus of post-ACLR rehabilitation, chronic quadriceps strength deficits often persist long after rehabilitation ends.[20,65,137] This sustained weakness may lead to chronic under loading of the surgical knee during both daily life and sport performance. As such, the distal femur may not receive adequate loading to stimulate an osteogenic response, and, in fact, may undergo bone loss. Full restoration of quadriceps performance may be necessary to mitigate BMD deficits in the distal femur following ACLR.

Another factor that may contribute to BMD deficits is altered movement biomechanics. Running is a fundamental human movement that is necessary across a multitude of sports. Running kinematics and kinetics of the surgical limb post-ACLR are significantly altered up to 12 months post-surgery in comparison with preinjury mechanics in collegiate athletes.[54] Further, significant asymmetries in running biomechanics have been observed up to five years post-ACLR.[87] During running, individuals post-ACLR demonstrate a chronic under loading of the surgical knee that may lead to reduced mechanical loading of the distal femur.[24] It has been postulated that altered knee loading patterns observed during walking and running may contribute to the onset and progression of OA.[17] Changes in distal femur BMD may, in fact, be a precondition of osteoarthritic changes, as subchondral BMD has been previously associated with OA in the general population.[8]

The purpose of this study was to evaluate the potential influence of isometric quadriceps performance and knee biomechanics during running on longitudinal changes in femoral BMD over the initial 2 years after ACLR in collegiate athletes. We hypothesized that reduced quadriceps performance and reduced knee kinematics and kinetics of the surgical limb would be associated with a greater BMD deficit at both the 5% and 15% regions of the distal femur.

Methods

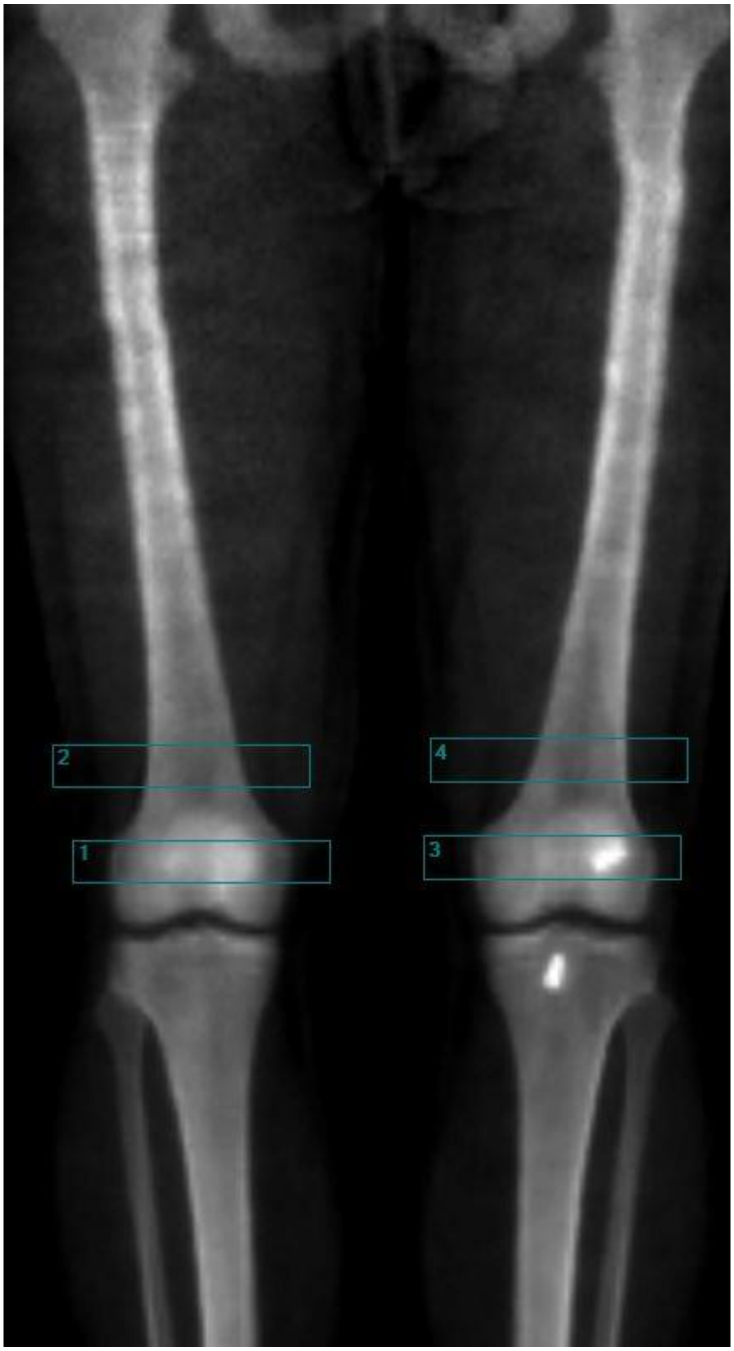
Participants

This study was a retrospective review of prospectively collected performance and healthcare data from NCAA Division I collegiate athletes at the University of Wisconsin-Madison between 2012 and 2022. Data of interest included serial post-ACLR whole-body DXA, isometric knee extensor torques, and running biomechanics testing. Records within the Badger Athletic Performance database were reviewed and records were extracted if the following criteria were met: the athlete 1) underwent a primary ACLR, 2) had no lower extremity surgery within 12 months before the primary ACLR, 3) had no internal hardware beyond typical ACLR fixation hardware, 4) had at least one whole-body DXA scan and isometric knee extensor torque testing or running analysis within 1 month of a given DXA scan, and 5) testing was completed between 3 and 24 months post-operatively. All eligible records for a given athlete were included, resulting in multiple observations for most athletes. If an athlete sustained a second ACL injury or underwent another lower extremity surgery, only data prior to the secondary injury/surgery were included in the analyses. This records review was approved by the university's Health Sciences Institutional Review Board.

DXA Assessment and Analysis

Whole-body DXA scans (pixel size = 2.4 x 3.0 mm) were performed using a single GE Healthcare Lunar iDXA densitometer and analyzed using enCORE software V.14.1 (Madison, WI, USA). All scans were acquired by an International Society for Clinical Densitometry (ISCD)–certified technologist and were reviewed by a physician with expertise in DXA analysis to ensure correct acquisition and interpretation. Femur length of the surgical limb was measured from the most superior aspect of the greater trochanter to the center of the intercondylar notch. Two ROIs, each 2 cm in height and spanning the width of the extremity, were centered at 5% and 15% of femur length (F5, F15) measured from the intercondylar notch (Figure 4.1). This methodology has been shown to be provide reproducible ROI placement.[53] The least significant change with 95% confidence for the F5 and F15 ROIs were found to be 0.134 g/cm^2 and 0.079 g/cm^2, respectively, based on a sample of healthy division I collegiate athletes (Supplemental Table 3.1, Appendix 2).[15] BMD output (g/cm^2) was recorded from these regions of the surgical limb and used in the subsequent analyses.

Figure 4.1. Representative dual-energy X-ray absorptiometry scan with custom regions of interest (ROIs). ROIs were 2 cm tall and spanned the width of the respective lower extremity. ROIs were positioned at 5% (boxes 1 and 3) and 15% (boxes 2 and 4) of the femur's length, measured from the distal femur. The bone mineral density (in g/cm^2) was extracted from each ROI for analysis.



Running Assessment and Analysis

Three-dimensional motion analysis was performed while athletes ran on an instrumented treadmill (Bertec Corporation, Columbus, OH). Fifty-two reflective markers (23 on anatomical landmarks) were placed on each athlete.[38] A static standing posture was used to identify hip joint centers and for model scaling. Kinematics were collected at 200 Hz using an 8-camera passive marker system (Motion Analysis Corporation, Santa Rosa, CA) synchronously with ground reaction forces (GRF), which were collected at 2000 Hz.

A standard protocol was utilized as follows: first, each athlete walked for a minimum of two minutes to acclimate to the treadmill and motion capture setup.[135] Athletes then ran with incremental increases in speed from 2.68 m/s to 4.47 m/s or until the athlete reached their self-reported maximum comfortable speed. Maximum comfortable speed was defined as the speed in which the athlete reported that they did not feel comfortable going any faster than. Kinematics and ground reaction forces were recorded for 15 seconds at each speed. The maximum comfortable speed was used for subsequent analyses. For an athlete with multiple observations, the maximum available speed that was consistent across all observations was selected to control for speed within an athlete.

Biomechanical modeling and inverse kinematic and dynamic routines were performed as previously described.[38] GRF and marker data were low-pass filtered using a bi-directional, 4th-order Butterworth filter with a cutoff frequency of 12 Hz. A 14-segment articular linkage that was scaled to the athlete's height, mass, and segment length was utilized to model the body. A 50 N threshold for vertical ground reaction force was used to identify initial foot contacts and toe-offs used for quantifying the stance phase of gait.[135] Peak knee flexion angle (PKF) and peak knee extensor moment (PKEM) during the stance phase normalized to body mass was calculated for each stride then averaged across 15 strides for the surgical limb for statistical analyses.

Isometric Strength Assessment and Analysis

Athletes completed isometric strength testing on an isokinetic dynamometer with the knee positioned at 90°, the hip positioned at 85°, and the knee adapter pad positioned 5 cm proximal to the medial malleolus in the reverse orientation to reduce compliance (Biodex System 4, Biodex Medical Systems, Shirley, NY).[73] Testing was performed on the non-surgical limb first. Athletes executed a progressive warmup (repetitions at 50%, 75%, and 90% of maximum effort) followed by two 5-second maximal voluntary isometric knee extension contractions (MVIC), while loud verbal encouragement and visual feedback of the torque signal were provided. MVIC trials were repeated if greater than a 10% difference was observed between trials. Torque was sampled at 2000 Hz, low-pass filtered using a bi-directional 3rd-order Butterworth filter with a cutoff frequency of 60 Hz, and baseline offset was removed. The peak knee extensor torque (PT) across two trials was identified using a custom Matlab script (Release 2018b, Mathworks, Inc., Natick, MA) and used for statistical analyses.

Following MVIC efforts, athletes remained in the same position and completed rapid voluntary isometric contractions. Trials were initiated by an auditory signal and athletes were instructed to kick as fast and as hard as possible[119] until torque production plateaued (2-3 seconds). A progressive warmup (repetitions at 50%, 75%, 90%, and 100% of maximum effort) was completed followed by a minimum of five recorded repetitions. Knee extensor efforts with a countermovement prior to the rise in torque were discarded.[118] The same signal processing scripts used for MVIC data were applied to the torque signals of the rapid voluntary efforts. The slope of the torque signal from 20% to 80% of peak torque was computed as the rate of torque development (RTD).[23] The best three of five recorded trials for each limb were averaged, which has been shown to maximize between-session reliability.[35] RTD values were normalized to the athlete’s mass and used for statistical analyses.

Statistical Analyses

Standard descriptive statistics (mean and standard deviation, frequency, and percentage) were used to describe the athlete population. The changes in femur BMD over time post-operatively in both the surgical and non-surgical limbs, irrespective of quadriceps performance and running mechanics, were assessed using linear mixed effects with limb as a fixed effect, sex as a covariate, and athlete and time as random effects. For the primary aim of this study, linear mixed effects models were used to assess the influence of quadriceps performance, running mechanics, and length of time post-operative (time) on surgical limb distal femur BMD. Sex was included in the models as a covariate. Athlete and time were assigned as random effects. Potential interactions between time and quadriceps performance or running mechanics were additionally assessed. For variables in which a significant interaction was detected, the estimated slopes of time were calculated at the mean, 1 standard deviation below the mean, and 1 standard deviation above the mean of the moderator and visualized with an interaction plot.[67] Multiple comparison adjustments were not made when exploring significant interactions. All analyses were performed using R (version 4.1.3; R Core Team) and significance was assessed at α ≤ .05.

Results

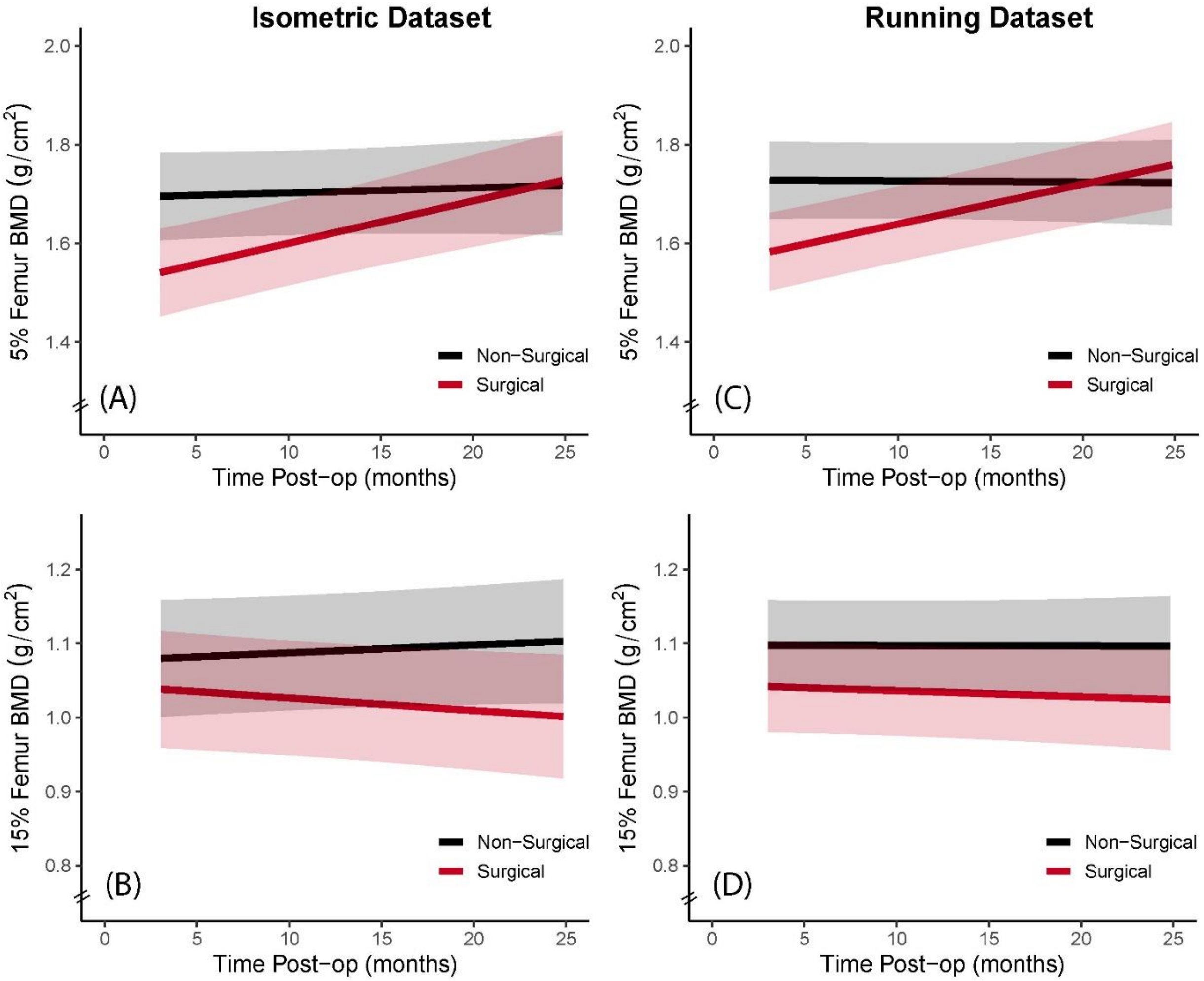
Following the records review process, 57 Division I collegiate athletes who underwent whole-body DXA scans between 3 and 24 months post-operative were identified. Of these, 43 athletes also had isometric knee extensor testing (105 observations) and 54 had running analyses (141 observations). Athletes participated in American football (n = 13), soccer (n = 13), basketball (n = 4), spirit (n = 3), track and field (n = 3), crew (n = 2), softball (n = 2), volleyball (n = 1), wrestling (n = 1), and tennis (n = 1) for the isometric and DXA dataset and American football (n = 18), soccer (n = 14), basketball (n = 5), spirit (n = 3), track and field (n = 3), softball (n = 3), wrestling (n = 3), crew (n = 2), volleyball (n = 2), and tennis (n = 1) for the running and DXA dataset. The number of observations for a given athlete ranged from 1 to 6 observations for both datasets, with an average of 2.4 ± 1.4 observations for isometric and DXA assessments and 2.6 ± 1.3 observations for running and DXA assessments (Supplemental Table 4.2, Appendix 3). The distribution of the number of observations over time post-ACLR can be found in Supplemental Table 4.3 (Appendix 3). The average running speed across all athletes was 3.73 ± 0.58 m/s, and 78% of athletes returned to sport, which was defined as returning to prior level of competition (Division I collegiate athletics). Further athlete demographics can be found in Table 4.1. Longitudinal changes in BMD of the 5% and 15% regions of both datasets, irrespective of quadriceps performance and running mechanics, are visualized in Figure 4.2. Significant interactions between limb and time were observed for the femur 5% ($p < .001$) and 15% ($p = .04$) ROIs of the isometric dataset and for the femur 5% ($p < .001$) but not the 15% ($p = 0.52$) ROI for the running dataset.

Table 4.1. Summary of athlete demographics.

Isometric and DXA		Running and DXA	
Participant Information (N = 43)[a]		Participant Information (N = 54)[a]	
	Values		Values
Total Observations	105	Total Observations	141
Age, y [b]	20.4 (1.5)	Age, y [b]	20.6 (1.6)
Body Mass, kg [b]	82.9 (18.8)	Body Mass, kg [b]	86.1 (18.9)
Height, m [b]	1.79 (0.10)	Height, m [b]	1.79 (0.10)
Body Mass Index, kg/m^2 [b]	25.7 (3.8)	Body Mass Index, kg/m^2 [b]	26.6 (4.5)
Females, n (% of total participants)	21 (48.8)	Females, n (% of total participants)	26 (47.3)
Graft type, n (% of total participants)		Graft type, n (% of total participants)	
Bone-patellar-tendon-bone	35 (81.4)	Bone-patellar-tendon-bone	46 (85.2)
Hamstring tendon	5 (11.6)	Hamstring tendon	5 (9.3)
Quadriceps tendon	3 (7.0)	Quadriceps tendon	3 (5.6)
Concomitant procedures, n (% of total participants)		Concomitant procedures, n (% of total participants)	
Meniscectomy	8 (17.8)	Meniscectomy	14 (25.9)
Meniscal repair	10 (22.2)	Meniscal repair	15 (27.8)
MPFL reconstruction	1 (2.2)	MPFL reconstruction	1 (1.9)
LCL reconstruction	1 (2.2)	LCL reconstruction	-
Time post-operatively, months		Time post-operatively, months	
Average	9.3 (5.3)	Average	9.8 (5.3)
Range	3.1, 24.8	Range	3.1, 24.8
Peak torque, Nm/kg		Peak knee flexion angle, °	
Surgical Limb	2.5 (0.7)	Surgical Limb	37.3 (6.0)
Non-Surgical Limb	3.3 (0.7)	Non-Surgical Limb	45.7 (4.6)
Rate of torque development, Nm/kg/s		Peak knee extensor moment, Nm/kg	
Surgical Limb	7.2 (3.3)	Surgical Limb	1.4 (0.5)
Non-Surgical Limb	13.1 (3.4)	Non-Surgical Limb	2.3 (0.4)
BMD 5% region of interest, g/cm^2		BMD 5% region of interest, g/cm^2	
Surgical Limb	1.74 (0.27)	Surgical Limb	1.76 (0.25)
Non-Surgical Limb	1.85 (0.26)	Non-Surgical Limb	1.85 (0.26)
BMD 15% region of interest, g/cm^2		BMD 15% region of interest, g/cm^2	
Surgical Limb	1.13 (0.22)	Surgical Limb	1.13 (0.20)
Non-Surgical Limb	1.19 (0.21)	Non-Surgical Limb	1.20 (0.21)

[a] Values are presented as mean (SD) unless otherwise indicated. DXA, dual-energy X-ray absorptiometry; MPFL, medial patellofemoral ligament; LCL, lateral collateral ligament; BMD, bone mineral density. [b] Based on first post-operative assessment.

Figure 4.2. Modeled changes between 3 and 24 months in bone mineral density (BMD) of the surgical (red) and non-surgical (black) limbs after ACLR in Division I collegiate athletes, adjusting for sex. Significant interactions between limb and time were observed for the femur 5% ($p < .001$, A) and 15% ($p = .04$, B) ROIs of the isometric dataset and for the femur 5% ($p < .001$, C) but not the 15% ($p = 0.52$, D) ROI for the running dataset.



5% Femur BMD

No significant interactions between time post-ACLR and PT ($p = .31$), RTD ($p = .98$), PKF ($p = .63$), or PKEM ($p = .75$) were detected for 5% femur BMD (Table 4.2). A significant main effect of time was observed for all variables (all p-values < .001) in which 5% femur BMD increased, on average, between 0.011 – 0.013 g/cm^2 per month over the initial 2 years post-ACLR (Table 4.2).

Table 4.2. Linear mixed effects model results for the effect of time post-operatively, knee extensor peak torque (PT), rate of torque development (RTD), running peak knee flexion angle (PKF), and running peak knee extensor moment (PKEM) on bone mineral density (BMD) at 5 and 15% of the distal femur. Sex was controlled in all models. CI, confidence interval

		Slope Estimate (95% CI)	p-value			Slope Estimate (95% CI)	p-value
5% BMD and PT	(Intercept)	1.443 (1.329, 1.557)	<0.001	5% BMD and PKF	(Intercept)	1.538 (1.381, 1.696)	<0.001
	Time	0.012 (0.007, 0.018)	<0.001		Time	0.011 (0.007, 0.015)	<0.001
	PT	0.009 (-0.020, 0.037)	0.56		PKF	0.000 (-0.004, 0.003)	0.83
5% BMD and RTD	(Intercept)	1.448 (1.339, 1.558)	<0.001	5% BMD and PKEM	(Intercept)	1.524 (1.425, 1.623)	<0.001
	Time	0.013 (0.008, 0.018)	<0.001		Time	0.011 (0.007, 0.015)	<0.001
	RTD	0.002 (-0.004, 0.007)	0.60		PKEM	0.000 (-0.038, 0.037)	0.98
15% BMD and PT	(Intercept)	1.087 (0.0982, 1.192)	<0.001	15% BMD and PKF	(Intercept)	1.173 (1.025, 1.320)	<0.001
	Time	-0.010 (-0.020, 0.000)	0.045		Time	-0.010 (-0.018, -0.001)	0.04
	PT	-0.024 (-0.055, 0.007)	0.13		PKF	-0.003 (-0.007, 0.000)	0.07
	Interaction	0.003 (0.000, 0.007)	0.048		Interaction	0.000 (0.000, 0.000)	0.04
15% BMD and RTD	(Intercept)	1.077 (0.985, 1.169)	<0.001	15% BMD and PKEM	(Intercept)	1.122 (1.038, 1.207)	<0.001
	Time	-0.010 (-0.016, -0.003)	0.004		Time	-0.007 (-0.011, -0.002)	0.004
	RTD	-0.005 (-0.012, 0.001)	0.12		PKEM	0.054 (0.013, 0.095)	0.01
	Interaction	0.001 (0.000, 0.002)	0.007		Interaction	-0.004 (-0.006, -0.001)	0.003

15% Femur BMD

Significant interactions between time post-ACLR and PT (p = .05), RTD (p = .007), PKF (p = .04), and PKEM (p = .003) were detected for 15% femur BMD (Table 4.2). Simple slope analyses were performed to explore significant interactions (Table 4.3, Figure 4.3). Athletes with a RTD below 7.20 Nm/kg/s (mean) at 9.3 months post-ACLR showed decreases in 15% femur BMD over time (p = .03). Similarly, athletes with PKEM below 0.92 Nm/kg (-1 SD) at 9.8 months post-ACLR showed decreases in 15% femur BMD over time (p =.02). Despite the significant interaction, simple slope analyses did not reveal significant differences at -1 SD below the mean for PT (1.75 Nm/kg, p = .07) and PKF (31.3°, p = .08).

Figure 4.3. Interaction plots for the effect of time post-operatively on 15% distal femur bone mineral density (BMD) when moderated by rate of torque development (RTD, A) and running peak knee extensor moment (PKEM, B). The moderator values were set at the mean and ± 1 standard deviation of each respective moderator.

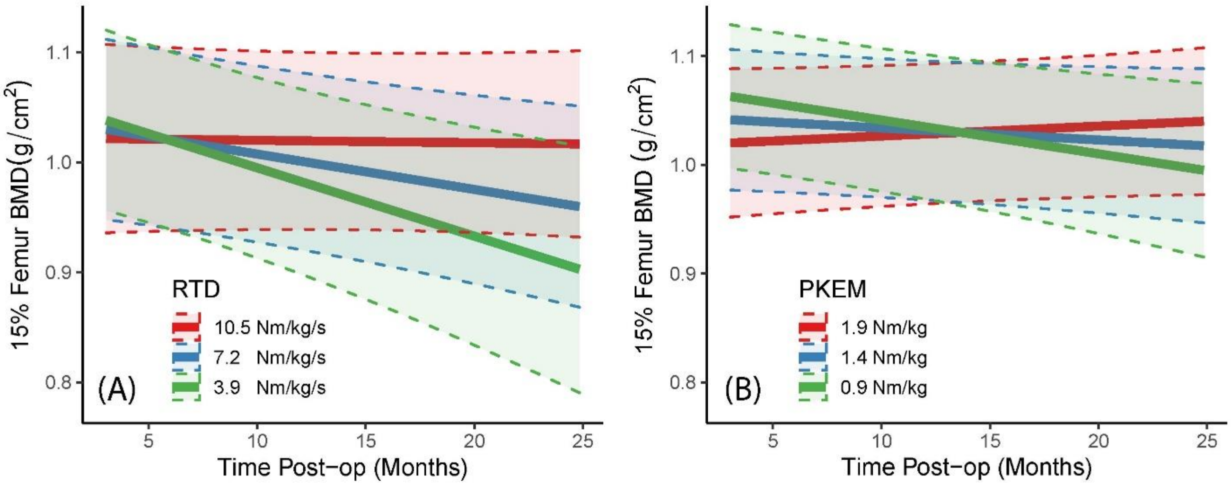


Table 4.3. Simple slope analysis for probing the interaction effects of knee extensor peak torque (PT), rate of torque development (RTD), running peak knee flexion angle (PKF), and running peak knee extensor moment (PKEM) on 15% distal femur bone mineral density (BMD). SD, standard deviation; CI, confidence interval

	Isometric Performance					
	PT			RTD		
	1.75 Nm/kg (-1 SD)	2.49 Nm/kg (Mean)	3.22 Nm/kg (+1 SD)	3.87 Nm/kg/s (-1 SD)	7.20 Nm/kg/s (Mean)	10.54 Nm/kg/s (+1 SD)
Slope	-0.004	-0.002	0.001	-0.006	-0.003	-0.0002
95% CI	(-0.009, 0.0002)	(-0.005, 0.001)	(-0.002, 0.004)	(-0.010, -0.002)	(-0.006, -0.0004)	(-0.003, 0.002)
p-value	0.07	0.25	0.57	0.01	0.03	0.87

	Running Biomechanics					
	PKF			PKEM		
	31.3° (-1 SD)	37.3° (Mean)	43.3° (+1 SD)	0.92 Nm/kg (-1 SD)	1.43 Nm/kg (Mean)	1.94 Nm/kg (+1 SD)
Slope	-0.002	-0.001	0.0003	-0.003	-0.001	0.001
95% CI	(-0.005, 0.0002)	(-0.003, 0.001)	(-0.002, 0.002)	(-0.006, -0.001)	(-0.003, 0.001)	(-0.001, 0.003)
p-value	0.08	0.31	0.75	0.02	0.20	0.37

Discussion

The purpose of this study was to evaluate the potential influence of isometric quadriceps performance and knee biomechanics during running on longitudinal changes in femoral BMD over the initial 2 years after ACLR in collegiate athletes. Partially consistent with our initial hypothesis, athletes with worse surgical limb quadriceps performance (lower RTD) demonstrated greater BMD loss at the 15% ROI of the distal femur over the first 2 years post-ACLR. Similarly, those who ran with lower PKEM in the surgical limb had greater BMD loss at the 15% ROI of the distal femur. Contrary to our initial hypothesis, isometric quadriceps performance and knee biomechanics during running did not have a significant effect on BMD at the 5% femur ROI.

Persistent distal femur BMD deficits have been observed following ACLR, even in patients who have returned to preinjury levels of activity.[53,88] To our knowledge this is the first study to link clinically modifiable factors to longitudinal changes in BMD post-ACLR. Bone mineral density at the 15% femur ROI had no association with time from surgery in athletes who achieved an RTD of 10.54 Nm/kg/s by ~9 months post-operatively. Our findings suggest that inadequate recovery of quadriceps performance has a detrimental effect on BMD of the distal femur following ACLR.

Quadriceps weakness is universal following ACLR, and a primary focus of post-operative rehabilitation is to restore quadriceps strength.[2,42] However, many individuals demonstrate persistent neuromuscular deficits at the time of return-to-sport and beyond.[65] The primary motor function of the quadriceps is to produce knee extensor torque. As the muscles originate at the anterior inferior iliac spine and proximal femur and insert on the tibial tuberosity via the patellar tendon, contractile force within the quadriceps generates compressive and shear forces about the distal femur.[75] Therefore, the positive relationship observed between quadriceps performance metrics and distal femur BMD may, in part, be due to the larger loads transferred to the bone by greater rate and magnitude of quadriceps contractile forces.

Similarly, during running, the compressive and shear forces acting on the distal femur tend to be greatest near midstance.[24] Greater knee flexion angles and larger knee extensor moments during running induce greater loads about the distal femur. Thus, altered running mechanics post-ACLR, with reduced PKF and PKEM, as seen in our population at 1 year post-operatively, may diminish recovery in distal femur BMD and lead to persistent deficits. Interventions aimed at promoting greater PKF and PKEM may increase forces about the distal femur, providing stimulus for bone density recovery in addition to improved neuromuscular function. Increasing stride length,[38] running at a faster speed,[98] or prescribing intermittent Groucho walking or running[76] are interventions that can elicit the desired increase in PKF and PKEM. It is feasible that restored running mechanics provides an additive effect to restored quadriceps extensor torque in distal femur BMD recovery, though we did not test this in our study. Certainly, it is important to ensure that an adequate level of quadriceps performance is restored prior to implementing gait retraining strategies, as better quadriceps performance has been associated with improved running mechanics in individuals following ACLR.[7,51,63,95] Gait retraining strategies aimed at promoting greater PKF and PKEM will likely have little effectiveness in the presence of significant quadriceps weakness.

It is important to highlight that the magnitude of change in femur BMD at the 15% region was more pronounced at varying levels of isometric quadriceps performance than running biomechanics. The difference in effort between tasks may explain these differences. Running is a submaximal task and does not require maximum quadriceps recruitment. As peak muscle force is associated with peak bone loads during running,[24,110] quadriceps force production may have the greatest influence on BMD of the distal femur, which is most accurately quantified via an isolated knee extensor contraction. Further, running does not provide optimal loading to stimulate an osteogenic response.[104] Bone cells lose the majority of their mechanosensivity after only 20 repetitive cycles of loading, thereby limiting the positive effect of running on bone development to the initial minutes of a run.[113,117,143] Other modes of exercise such as hopping or jumping may induce greater forces about the distal femur and as a result, demonstrate a stronger relationship to BMD changes following ACLR than running.

Prior work has demonstrated that bone within the F5 region responds differently after ACLR than the F15 region.[53] This previous study used identical scan processing methods as the current study and found that the F5 region demonstrated an initial decline in BMD compared to preinjury, but recovered to preinjury levels by 24 months post-ACLR. A similar recovery over the initial 24 months post-ACLR was noted in the current study albeit to a greater magnitude. This variation in magnitude may be attributed to the inherent variability of assessing BMD at the F5 region with a whole-body DXA scan, as this region encompasses most of the patella and surgical hardware. We are confident that the directionality of BMD change within the F5 region is correct as the change exceeds the least significant change level (0.134 g/cm^2), but the magnitude may be inflated particularly due to the increased variability in this region and fewer data points at later time points post-operatively. As such, the magnitude of change in BMD over time of the F5 region should be interpreted with caution.

Although this study demonstrated a unique relationship between clinically modifiable factors and BMD changes post-ACLR, it is not without limitations. Activity levels and rehabilitation were not controlled in this study; however, most athletes (78%) returned to full sports participation at the NCAA Division I collegiate level and underwent rehabilitation in the same sports medicine facility under standardized post-operative protocols. Not all athletes completed testing out to 2 years post-operatively. Due to fewer tests between 12 and 24 months compared to before 12 months post-ACLR, we had reduced statistical power at the later time points. To account for the variation in number of observations for a given athlete over time, linear mixed-effects models were used. Additionally, most athletes included in this study underwent ACLR with a bone-patellar tendon-bone graft. As such, findings may not generalize to other graft types. While the independent variables of interest (isometric quadriceps performance and running biomechanics) are clinically modifiable factors, they are not direct measures of bone loads. A more detailed musculoskeletal modeling approach may elicit a better understanding of the mechanical stresses at the distal femur. Further, the cutoffs used to assess the interaction effect between isometric quadriceps performance and running biomechanics were chosen based on the distribution of the variables and should not be used clinically. It is important to note that BMD values for this study were acquired using whole-body DXA scans. Whole-body DXA scans may not be as precise in estimating local BMD as site-specific scans. For the F15 ROI, only the estimated interaction effects at the level of -1 standard deviation for RTD exceeded the least significant change (0.079 g/cm^2) over the initial 2 years post-ACLR. As such, the interactions effects for other levels and running mechanics should be interpreted with caution as they did not exceed this threshold.

In conclusion, surgical limb RTD and PKEM during running were significantly associated with longitudinal changes in distal femur BMD (15%) of NCAA Division I collegiate athletes following ACLR. Worse quadriceps performance and running mechanics were associated with a greater BMD loss of the distal femur between 3 and 24 months post-operatively. These findings suggest that restoring quadriceps performance and knee biomechanics during running following ACLR may limit distal femur bone loss post-ACLR.

Conclusion

The culmination of chapters included in this thesis highlight the lingering abnormalities in knee biomechanics during running following ACLR, identify potential modifiable factors associated with running mechanics, and illuminate the potential impact deficits in running knee biomechanics and quadriceps neuromuscular performance have on bone health. Collegiate athletes following ACLR demonstrate persistent deficits in surgical knee kinematics and kinetics during running compared to preinjury levels.[54] Interestingly, with an increase in running speed, knee kinematics and kinetics increased similarly in both limbs at 4-7 months and 8-12 months post-ACLR, yet significant between-limb differences remained. Fortunately, recovery in quadriceps performance (quadriceps strength and rate of torque development) were associated with recovery in knee biomechanics during running. However, despite adequate quadriceps resolution, deficits in running biomechanics remained. Statistically significant relationships between bone changes following ACLR and knee biomechanics during running were observed, but the magnitude of these effects were minimal and may simply be due to measurement error. Nevertheless, quadriceps rate of torque development was found to be associated with bone changes and this effect was greater than measurement error.

Findings from this thesis have direct clinical implications. First and foremost, altered surgical knee biomechanics during running are nearly universal across athletes and last beyond the typical time of return to sport. Therefore, in a traditional clinical setting, where 3-dimensional motion analysis is uncommon, it is reasonable to assume that athletes post-ACLR run with significant asymmetries. Interestingly, the non-surgical limb knee mechanics stayed relatively stable throughout the first 12 months post-ACLR as compared to preinjury levels. This suggests that the non-surgical limb can serve as a valid reference when preinjury biomechanics are unavailable, which is rare. Further, peak knee flexion angle deficits were substantial at 12 months post-ACLR (9° less than preinjury levels, on average). This magnitude of deficit is feasible to detect in a clinical setting by simply using 2-dimension video analysis.[108,125,149] Recording the sagittal view of an athlete running on a treadmill with a standard video camera (120+ frames per second) and comparing the peak knee flexion angles of the surgical and non-surgical limb is a practical approach for objectively assessing running mechanics in a standard physical therapy clinic. Lack of asymmetry detected using this methodology does not guarantee symmetrical running mechanics, but is an excellent first line of defense to detect substantial asymmetries. It is likely that in the near future, wearable technology and/or markerless motion capture analysis will be more readily available in a clinic setting and will greatly enhance rehabilitation professionals' ability to objectively assess running biomechanics in athletes post-ACLR.

Although the work included in this dissertation does not directly answer the question of when it is safe to resume running, it does begin to raise questions about current clinical practice of returning athletes to running by 12-16 weeks post-operatively. At 12-16 weeks post-ACLR in athletes included in this thesis, substantial deficits in quadriceps strength and rate of torque development were present (many athletes below 50% LSI). Initiating running post-ACLR without adequate quadriceps torque generating capacity may lead athletes to adopt maladaptive movement strategies. These maladaptive movement strategies may become ingrained and persist long-term post-ACLR.[87] Recovery in quadriceps performance was found to be associated with improvement in both running mechanics and bone mineral density of the distal femur post-ACLR. Therefore, waiting longer post-operatively and/or utilizing quadriceps strength and rate of torque development as objective measures to guide when it is appropriate to resume running may be warranted. Unfortunately, definitive levels of quadriceps performance necessary for guiding when it is acceptable to resume running is not known. Recently, there has been efforts to determine quadriceps strength cutoffs,[21,36,44] but these studies did not consider running biomechanics and have a high likelihood of bias based on the study design. Comparing the knee torque generated during an isometric task (quadriceps strength and RTD) with the torque generated during running (peak knee extensor moment and rate of knee extensor moment) at multiple speeds in healthy athletes may be a good starting point to determine the percentage of isometric torque typically utilized during running. However, a clinical trial, assessing the influence of holding athletes from running until specific objective criteria are met (e.g. quadriceps strength of 60, 70, or 80% LSI; or surgical limb strength of 1.5, 2.0, or 2.5 Nm/kg) following ACLR is needed to directly answer this question.

Unlike quadriceps strength, rate of torque development is challenging to assess clinically as it currently requires a rigid system, low signal-to-noise ratio, and a high sampling rate.[73] However, our lab has been working on validating methods to assess rate of torque development in a more clinically feasible manner. Our preliminary findings (unpublished data) demonstrate excellent agreement between the rate of torque development methods included in this thesis (slope from 20-80% of peak torque during a rapid isometric contraction sampled at 2000 Hz) and the same methods applied to a down sampled torque signal (100 Hz, standard electromechanical dynamometer sampling rate). Future work focusing on translating these methods to more affordable handheld dynamometers or in-line pull load cells will greatly enhance the clinical impact of the work presented in this thesis.

It is important to highlight that the relationship between quadriceps performance and knee biomechanics during running was not 1-to-1. Even with full quadriceps resolution, it is likely that athletes will still demonstrate abnormal running mechanics.[6] Consequently, there is a need for developing strategies to target specific running gait impairments post-ACLR, namely, reduced peak knee flexion angles and moments of the surgical limb. Chapter 2 of this thesis highlighted that speed may be used to promote greater knee flexion angles and moments; however, large between-limb asymmetries remained. To further address the typical impairments in running biomechanics post-ACLR, a range of interventions may be helpful and need further exploration. Biofeedback on movement mechanics may be the most direct way to target the observed impairments. Specific to walking, participants were able to modify mechanics based on real-time biofeedback of ground reaction forces[27] and knee moments.[83] Adapting these methods to running is an important future line of inquiry. Unfortunately, most methods of providing real-time biofeedback are constrained to a laboratory setting. Assessing the utility of wearable devices that are able to provide real-time feedback on movement mechanics may be a more clinically feasible option. Additionally, minimal tech options may be just as successful, such as reducing cadence or specific verbal cues combined with post-practice video feedback. Reducing cadence has been shown to increase the knee extensor demands during running in healthy athletes.[38] However, this effect needs to be formally assessed in athletes following ACLR.

The direct clinical implications of bone loss surrounding the reconstructed knee are not well understood at this point. It is plausible that bone loss increases the risk of sustaining a periprosthetic fracture following a total knee arthoplasty.[55] Further, subchondral BMD and subchondral bone plate changes at the knee have been associated with the development of osteoarthritis in the general population[8]; however, this relationship has not been explored in bone further away from the joint surface, such as the 15% femur region. Future work will aim to establish the relationship between bone changes more removed from the joint line and measures of cartilage health. Moreover, there is a need to further validate the total-body DXA analyses presented as part of this thesis. Total-body DXA scans were selected out of convenience, as they provide information beyond BMD surrounding the knee (e.g. total-body BMD, body composition) and were collected as part of the standard of care within Badger Athletic Performance. Knee-specific DXA scans (pixel size = 0.3 x 0.24 mm) provide a more precise measure of BMD than total-body (pixel size = 2.4 x 3.0 mm). Over the last year both total-body and knee-specific DXA scans on both healthy collegiate athletes and those following ACLR have been collected. The agreement between the two scan types, for measuring the 5 and 15% of femur and tibia BMD, will be assessed and will determine if total-body scans provide a comparable measure of BMD. These findings will help support the methodology used in future studies related to BMD following ACLR.

As the data included in this thesis were collected on athletes throughout the rehabilitation process and out to 2 years post-ACLR, findings are relevant to a time where rehabilitation professionals can easily intervene. However, we do not currently have consistent data on athletes beyond 2 years post-ACLR. There is a need to follow up athletes long-term, even beyond their time in sport, and assess the same metrics presented in this thesis, with the addition of measures of cartilage health. Planning is underway for formally assessing the long-term joint health of former collegiate athletes with a history of ACLR. This work will focus on identify potential clinically modifiable factors that are associated with worse cartilage health in former collegiate athletes, as osteoarthritis is a significant concern in this population.[37,70,142] Specifically, athletes between 2-20 years post-ACLR will be recruited in addition to a matched healthy control group. Each participant will complete 1) MRI imaging of knee cartilage (GE 3D MAPPS T2 and T1rho sequences) and lower extremity muscle volumes; 2) dual energy x-ray absorptiometry scans; 3) three-dimensional motion analysis during walking, running, and jumping; 4) isometric knee extensor testing; 5) patient reported outcomes (PROs) for overall health, knee specific function, kinesiophobia, and physical activity levels. The aim of this project is to assess the impact ACLR in former collegiate athletes has on between-limb symmetry of bone mineral density (BMD), muscle volume, neuromuscular performance, knee biomechanics (walking, running, and jumping), and cartilage health compared to matched, uninjured former collegiate athletes. Also, differences in levels of physical activity and quality of life will be explored between groups. An additional aim is to identify if BMD, muscle volume, neuromuscular performance, knee biomechanics, physical activity levels, and quality of life are associated with cartilage health in former collegiate athletes post-ACLR.

Running related research in individuals following ACLR is a relatively understudied topic within the well-studied, ACL field. This provides a unique opportunity to leverage the literature related to ACL injuries and apply it to the task of running. As running is a primary component of multiple sports and commonly used to maintain an active, healthy lifestyle,[33] it is a particularly relevant task to individuals post-ACLR. From a cartilage perspective, running introduces significantly greater joint contact forces than walking.[79] As such, the relatively large and persistent alterations observed in knee mechanics during running post-ACLR may contribute to the increased prevalence of post-traumatic knee osteoarthritis.[3,17,37,70,142] There are vast opportunities to expand on the running related research in individuals following ACLR.

Ultimately, the work included in this thesis provides strong evidence of persistent abnormalities in knee biomechanics during running compared to preinjury biomechanics. Additionally, the work highlights the relationship between running biomechanics and clinical and physiological measures, some of which may be future targets used to modify knee biomechanics during running (e.g. quadriceps performance and running speed). As research in this area expands and more objective measures of running biomechanics and quadriceps performance are translated to the clinical setting, the clinical impact of this work will be significantly enhanced.

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Appendix 1.

Supplemental File 2.1. Sensitivity analysis for the influence of maximal speed achieved on the effect of speed on knee biomechanics

Purpose

Not all athletes identified for inclusion in this study achieved the fastest running speed (4.47 m/s). Including data for athletes that did not achieve all speeds may confound the results. As such, a sensitivity analysis was performed to assess the influence of including athletes in the complete dataset (completing running analysis at 2 different speeds) compared to a reduced dataset comprised of only those that achieved at least 3.80 m/s.

Methods

Multivariable linear mixed effects models assessed the influence of speed and limb on biomechanics during running on both the full and reduced datasets. Speed (5 levels) and limb (2 levels) were treated as categorical variables. Athlete and limb post-ACLR were assigned as random effects (limb nested within athlete). The interaction between speed and limb was assessed for significance and retained if significant. Least squares means and associated 95% confidence intervals were calculated. The difference between least square means for each limb and speed between the two models were calculated to assess the difference between the two datasets. This process was conducted for both peak knee flexion angle and peak knee extensor moment at both the early (4-7 months) and late (8-12 months) post-ACLR.

Results

4-7 Months post-ACLR

In total, 41 athletes were identified for inclusion in the study irrespective of speed achieved. When the criteria of achieving at least 3.80 m/s was applied, the number of athletes was reduced to 28.

Table S1. Least square mean values of peak knee extensor moment for the full model at the 4-7 month time point.

Peak Knee Extensor Moment (PKEM)					
Limb	Speed (m/s)	PKEM (Nm/kg)	SE	UCL	LCL
Non-Surgical	2.68	2.11	0.0796	2.27	1.952
Surgical	2.68	1.06	0.0796	1.22	0.9
Non-Surgical	2.95	2.19	0.0797	2.35	2.032
Surgical	2.95	1.14	0.0797	1.3	0.979
Non-Surgical	3.35	2.3	0.0796	2.45	2.137
Surgical	3.35	1.24	0.0796	1.4	1.085
Non-Surgical	3.80	2.39	0.0802	2.55	2.235
Surgical	3.80	1.34	0.0802	1.5	1.183
Non-Surgical	4.47	2.5	0.0812	2.66	2.336
Surgical	4.47	1.45	0.0812	1.61	1.284

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S2. Least square mean values of peak knee extensor moment for the reduced model (3.80 m/s or faster) at the 4-7 month time point.

Peak Knee Extensor Moment (PKEM)					
Limb	Speed (m/s)	PKEM (Nm/kg)	SE	UCL	LCL
Non-Surgical	2.68	2.08	0.105	2.29	1.871
Surgical	2.68	1.1	0.105	1.31	0.889
Non-Surgical	2.95	2.17	0.105	2.38	1.96
Surgical	2.95	1.19	0.105	1.4	0.978
Non-Surgical	3.35	2.27	0.105	2.48	2.062

Surgical	3.35	1.29	0.105	1.5	1.081
Non-Surgical	3.80	2.37	0.105	2.58	2.16
Surgical	3.80	1.39	0.105	1.6	1.178
Non-Surgical	4.47	2.47	0.105	2.68	2.262
Surgical	4.47	1.49	0.105	1.7	1.28

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S3. Difference in least square mean values of peak knee extensor moment (Nm/kg) between the full and reduced model at the 4-7 month time point.

	2.68 m/s		2.95 m/s		3.35 m/s		3.80 m/s		4.47 m/s	
	Non	Surg	Non	Surg	Non	Surg	Non	Surg	Non	Surg
PKEM difference (Nm/kg)	-0.03	0.04	-0.02	0.05	-0.03	0.05	-0.02	0.05	-0.03	0.04

Non, Non-Surgical; Surg, Surgical

Table S4. Least square mean values of peak knee flexion for the full model at the 4-7 month time point.

Peak Knee Flexion (PKF)					
Limb	Speed (m/s)	PKF (°)	SE	LCL	UCL
Non-Surgical	2.68	44.0	0.864	42.3	45.7
Surgical	2.68	32.8	0.864	31.1	34.5
Non-Surgical	2.95	44.5	0.865	42.8	46.2
Surgical	2.95	33.8	0.865	32.1	35.6
Non-Surgical	3.35	45.3	0.864	43.6	47
Surgical	3.35	34.9	0.864	33.1	36.6

Non-Surgical	3.80	45.8	0.878	44	47.5
Surgical	3.80	35.9	0.878	34.2	37.7
Non-Surgical	4.47	45.9	0.903	44.1	47.7
Surgical	4.47	37.3	0.903	35.5	39.1

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S5. Least square mean values of peak knee flexion for the reduced model (3.80 m/s or faster) at the 4-7 month time point.

Peak Knee Flexion (PKF)					
Limb	Speed (m/s)	PKF (°)	SE	LCL	UCL
Non-Surgical	2.68	43.3	1.13	41	45.5
Surgical	2.68	33.3	1.13	31	35.6
Non-Surgical	2.95	43.9	1.13	41.6	46.2
Surgical	2.95	34.3	1.13	32	36.6
Non-Surgical	3.35	44.7	1.13	42.4	47
Surgical	3.35	35.3	1.13	33.1	37.6
Non-Surgical	3.80	45.2	1.13	42.9	47.4
Surgical	3.80	36.4	1.13	34.2	38.7
Non-Surgical	4.47	45.3	1.15	43	47.6
Surgical	4.47	37.8	1.15	35.5	40.1

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S6. Difference in least square mean values of peak knee flexion (°) between the full and reduced model at the 4-7 month time point.

	2.68 m/s		2.95 m/s		3.35 m/s		3.80 m/s		4.47 m/s	
	Non	Surg	Non	Surg	Non	Surg	Non	Surg	Non	Surg

PKF difference (°)	-0.7	0.5	-0.6	0.5	-0.6	0.4	-0.6	0.5	-0.6	0.5

Non, Non-Surgical; Surg, Surgical

8-12 Months post-ACLR

In total, 42 athletes were identified for inclusion in the study irrespective of speed achieved. When the criteria of achieving at least 3.80 m/s was applied, the number of athletes was reduced to 31.

Table S7. Least square mean values of peak knee extensor moment for the full model at the 8-12 month time point.

Peak Knee Extensor Moment (PKEM)					
Limb	Speed (m/s)	PKEM (Nm/kg)	SE	UCL	LCL
Non-Surgical	2.68	2.11	0.068	2.24	1.97
Surgical	2.68	1.3	0.068	1.43	1.16
Non-Surgical	2.95	2.21	0.0682	2.35	2.08
Surgical	2.95	1.41	0.0682	1.54	1.27
Non-Surgical	3.35	2.3	0.0681	2.44	2.17
Surgical	3.35	1.5	0.0681	1.63	1.36
Non-Surgical	3.80	2.39	0.0686	2.53	2.26
Surgical	3.80	1.59	0.0686	1.73	1.45
Non-Surgical	4.47	2.47	0.069	2.6	2.33
Surgical	4.47	1.66	0.069	1.8	1.52

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S8. Least square mean values of peak knee extensor moment for the reduced model (3.80 m/s or faster) at the 8-12 month time point.

Peak Knee Extensor Moment (PKEM)					
Limb	Speed (m/s)	PKEM (Nm/kg)	SE	UCL	LCL
Non-Surgical	2.68	2.18	0.0842	2.35	2.01
Surgical	2.68	1.33	0.0842	1.5	1.17
Non-Surgical	2.95	2.28	0.0843	2.45	2.11
Surgical	2.95	1.44	0.0843	1.61	1.27
Non-Surgical	3.35	2.37	0.0842	2.54	2.2
Surgical	3.35	1.53	0.0842	1.7	1.36
Non-Surgical	3.80	2.46	0.0842	2.63	2.29
Surgical	3.80	1.62	0.0842	1.79	1.45
Non-Surgical	4.47	2.54	0.0846	2.7	2.37
Surgical	4.47	1.69	0.0846	1.86	1.52

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S9. Difference in least square mean values of peak knee extensor moment (Nm/kg) between the full and reduced model at the 4-7 month time point.

	2.68 m/s		2.95 m/s		3.35 m/s		3.80 m/s		4.47 m/s	
	Non	Surg	Non	Surg	Non	Surg	Non	Surg	Non	Surg
PKEM difference (Nm/kg)	0.07	0.03	0.07	0.03	0.07	0.03	0.07	0.03	0.07	0.03

Non, Non-Surgical; Surg, Surgical

Table S10. Least square mean values of peak knee flexion for the full model at the 8-12 month time point.

Peak Knee Flexion (PKF)					
Limb	Speed (m/s)	PKF (°)	SE	LCL	UCL
Non-Surgical	2.68	44.3	0.773	42.7	45.8
Surgical	2.68	36	0.773	34.4	37.5
Non-Surgical	2.95	44.9	0.778	43.4	46.5
Surgical	2.95	37	0.778	35.5	38.6
Non-Surgical	3.35	45.4	0.775	43.8	46.9
Surgical	3.35	37.9	0.775	36.3	39.4
Non-Surgical	3.80	45.7	0.786	44.1	47.3
Surgical	3.80	38.6	0.786	37.1	40.2
Non-Surgical	4.47	45.8	0.793	44.2	47.3
Surgical	4.47	39.3	0.793	37.8	40.9

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S11. Least square mean values of peak knee flexion for the reduced model (3.80 m/s or faster) at the 8-12 month time point.

Peak Knee Flexion (PKF)					
Limb	Speed (m/s)	PKF (°)	SE	LCL	UCL
Non-Surgical	2.68	44.6	0.961	42.7	46.6
Surgical	2.68	36.2	0.961	34.3	38.1
Non-Surgical	2.95	45	0.961	43.1	46.9
Surgical	2.95	37.3	0.961	35.4	39.2
Non-Surgical	3.35	45.6	0.961	43.7	47.6

Surgical	3.35	38.2	0.961	36.3	40.2
Non-Surgical	3.80	45.8	0.961	43.9	47.8
Surgical	3.80	38.9	0.961	37	40.9
Non-Surgical	4.47	46	0.97	44	47.9
Surgical	4.47	39.6	0.97	37.7	41.6

SE, standard error; UCL, upper 95% confidence level; LCL lower 95% confidence level

Table S12. Difference in least square mean values of peak knee flexion (°) between the full and reduced model at the 8-12 month time point.

	2.68 m/s		2.95 m/s		3.35 m/s		3.80 m/s		4.47 m/s	
	Non	Surg	Non	Surg	Non	Surg	Non	Surg	Non	Surg
PKF difference (°)	0.3	0.2	0.1	0.3	0.2	0.3	0.1	0.3	0.2	0.3

Non, Non-Surgical; Surg, Surgical

Conclusion

This sensitivity analysis demonstrated that including all athletes in the dataset, regardless of running speed achieved, had minimal influence on the least square mean estimates. Additionally, the 95% confidence intervals were reduced when using the full model compared to the reduced model. Findings were similar at both the early and late time points post-ACLR. Therefore, we proceeded with the full dataset for this study.

Appendix 2.

Supplemental Table 3.1. Distribution of the number of observations over time post-anterior cruciate ligament reconstruction (ACLR).

Observations between 3-24 months Post-ACLR						
3-6 months	6-9 months	9-12 months	12-15 months	15-18 months	18-21 months	21-24 months
24	35	17	20	12	6	9

Supplemental Table 3.2. Linear mixed effects model results for the effect of time post-anterior cruciate ligament reconstruction (Time) and knee extensor peak torque limb symmetry index (PT_{LSI}) on peak knee flexion difference (PKF_{DIFF}) and peak knee extensor moment limb symmetry index ($PKEM_{LSI}$). A negative PKF_{DIFF} represents reduced knee flexion on the surgical limb. Marginal R^2 for the PKF_{DIFF} model was 0.42 and for the $PKEM_{LSI}$ model was 0.36.

		Estimate (95% CI)	p-value	Partial R^2 (95% CI)
PKF_{DIFF} (°)	(Intercept)	-18.06 (-20.95, -15.18)	<0.001	
	PT_{LSI} (%)	0.09 (0.04, 0.14)	<0.001	0.10 (0.02, 0.22)
	Time (months)	0.36 (0.19, 0.54)	<0.001	0.12 (0.03,0.25)
$PKEM_{LSI}$ (%)	(Intercept)	24.54 (13.30, 35.78)	<0.001	
	PT_{LSI} (%)	0.30 (0.12, 0.48)	0.001	0.06 (0.00, 0.17)
	Time (months)	1.65 (0.83, 2.48)	0.001	0.13 (0.04, 0.26)

CI, confidence interval

Supplemental Table 3.3. Linear mixed effects model results for the effect of time post-anterior cruciate ligament reconstruction (Time) and rate of torque development limb symmetry index (RTD_{LSI}) on peak knee flexion difference (PKF_{DIFF}) and peak knee extensor moment limb symmetry index ($PKEM_{LSI}$). A negative PKF_{DIFF} represents reduced knee flexion on the surgical limb. Marginal R^2 for the PKF_{DIFF} model was 0.48 and for the $PKEM_{LSI}$ model was 0.47.

		Estimate (95% CI)	p-value	Partial R^2 (95% CI)
PKF_{DIFF} (°)	(Intercept)	-16.30 (-18.37, -14.23)	<0.001	
	RTD_{LSI} (%)	0.11 (0.07, 0.14)	<0.001	0.25 (0.12, 0.38)
	Time (months)	0.25 (0.10, 0.41)	0.003	0.08 (0.01, 0.20)
$PKEM_{LSI}$ (%)	(Intercept)	28.00 (20.39, 35.62)	<0.001	
	RTD_{LSI} (%)	0.38 (0.25, 0.51)	<0.001	0.20 (0.08, 0.33)
	Time (months)	1.30 (0.62, 1.98)	0.001	0.11 (0.03, 0.24)

CI, confidence interval

Appendix 3.

Supplemental Table 4.1. Least significant change (LSC) with 95% precision of the femur 5% and femur 15% regions of interest (ROI). Data comes from 30 healthy limbs of collegiate athletes (Sex: 7 Female, 8 Male; Sport: 10 basketball, 3 hockey, and 2 golf; Age: 20.4 ± 1.1; Height: 1.81 ± 0.13 m; Mass: 77.2 ± 14.0 kg; BMI: 23.3 ± 1.9) from a prior published manuscript.[15]

	Least significant change (LSC) with 95% precision	
	Root-mean-square deviation (g/cm^2)	Coefficient of variation (%)
Femur 5% ROI	0.134	7.03
Femur 15% ROI	0.079	6.91

Supplemental Table 4.2. Distribution of the number of observations for a given athlete post-anterior cruciate ligament reconstruction (ACLR) for both datasets. DXA, Dual energy X-Ray Absorptiometry

	Observations for a given athlete post-ACLR					
	1	2	3	4	5	6
DXA + Isometric	16	7	10	6	3	1
DXA + Running	14	11	17	7	4	1

Supplemental Table 4.3. Distribution of the number of observations over time post-anterior cruciate ligament reconstruction (ACLR) for both datasets. DXA, Dual energy X-Ray Absorptiometry

	Observations between 3-24 months Post-ACLR						
	3-6 months	6-9 months	9-12 months	12-15 months	15-18 months	18-21 months	21-24 months
DXA + Isometric	30	37	17	8	5	0	8
DXA + Running	36	46	22	19	6	2	10