GAIT BIOMECHANICS AND QUADRICEPS MUSCLE FUNCTION ACROSS ACL RECONSTRUCTION CHRONICITY

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ABSTRACT

Background: Following anterior cruciate ligament reconstruction (ACLR) surgery, patients often experience chronic knee disability characterized by self-reported chronic knee dysfunction and an elevated risk for developing early onset knee joint degeneration. Post-traumatic adaptations in musculoskeletal function, including abnormal lower-extremity gait biomechanics, impairments in quadriceps muscle function, and underlying neural adaptations is proprioception, may contribute towards the development of chronic knee disability. Timely detection of potential deleterious adaptations in musculoskeletal function may allow clinicians the opportunity to intervene and potentially slow the adverse effects on knee joint function; however, there is currently limited understanding of when adaptations in muscle function actually develop over the course of time post-surgery. The overall purpose of these projects were to examine gait biomechanics, submaximal quadriceps muscle control, and the effects of vibration on muscle function in individuals with a history of ACLR at sequential time-frames post-surgery. **Methods:** ACLR participants were stratified into groups based on time post-surgery, Early (<2 years), Mid (2-5 years), Late (5-15 years), and healthy individuals participated as healthy controls. Walking and jogging knee and hip kinetics and kinematics were collected using three-dimensional motion capture analysis and inter-limb differences were evaluated with in group. Submaximal quadriceps force control was measured during isometric, concentric, and eccentric force-matching tasks at 25% of maximum contraction and force variability and error were calculated. Quadriceps strength was measured at baseline and following a 20-minute patellar tendon vibration intervention and the change in quadriceps strength was calculated. **Results:** The Early group demonstrated the inter-limb differences in frontal and sagittal plane knee and hip kinetics and kinematics, the Late

group demonstrated inter-limb differences in frontal plane knee and hip kinetics, and the Mid groups and controls had no significant differences between limbs for any gait variables. Knee adduction moment was lower in the Early group but higher in the Late group. ACLR knees demonstrated lower force variability and error during concentric contractions than controls. Lower variability and error were correlated with lower physical activity levels in ACLR knees but not time post-surgery. Vibration increased quadriceps strength in ACLR knees and controls. Effect sizes for raw-change indicated ACLR knee experienced an attenuated increased in quadriceps strength post-vibration than controls. Earlier time post-surgery was correlated with an attenuated response to vibration. **Conclusions:** We observed altered gait biomechanics, submaximal quadriceps force control, and response to tendon vibration in ACLR groups compared to controls. Time post-surgery may play a role in the presentation of post-traumatic adaptations in muscle function. Our most interesting findings suggest that there may be a pattern in knee adduction moments during gait from a reduced moment early after surgery to an increased knee adduction moment later after surgery.

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APPROVAL OF THE DISSERTATION

This dissertation, Gait Biomechanics and Quadriceps Muscle Function across ACL Reconstruction Chronicity, has been approved by the Graduate Faculty of the Curry School of Education in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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SECTION II: MANUSCRIPT I

WALKING AND JOGGING BIOMECHANICS AT EARLY, MID, AND LATE TIME-FRAMES AFTER ACL RECONSTRUCTION

ABSTRACT

Background: Adaptations in lower-extremity gait biomechanics during walking and jogging have been reported in patients with a history of anterior cruciate ligament reconstruction (ACLR). Over time, adaptations in knee joint loading may contribute to the development of knee joint degeneration. There is limited understanding of how gait adaptations may present in patients at different time-frames after ACLR. **Methods:** Participants included ACLR patients stratified into Early (6-month to 2-years, n=18), Mid (2-5years, n=20), and Late (5-15 years, n=20) ACLR groups based on time post-surgery and a healthy control group (n=20). Walking and jogging motion capture analysis was performed on all subjects. Sagittal and frontal knee and hip kinetics and kinematics were measured on the involved and uninvolved limbs and inter-limb comparison were made across the gait cycle by plotting graphs of means and 90% confidence intervals separately in each group. Significant differences between limbs we determined as a consecutive 3% of the gait cycle in which 90% confidence intervals did not overlap. **Results:** During walking and jogging, the Early ACLR group demonstrated lower sagittal and frontal knee and hip kinetics in ACLR limb compared to the uninvolved, the Late ACLR group demonstrated greater frontal plane knee and hip kinetics in the ACLR limb compared to uninvolved, and the Mid ACLR group and Control group did not demonstrate inter-limb gait differences. All differences were supported by large effect sizes with 95% confidence intervals that did not cross zero. **Conclusions:** The Early ACLR group demonstrated decreased joint loading on the ACLR limb, which may suggest a protective gait pattern in the early years after surgery. The Mid ACLR group did not demonstrate gait asymmetries, suggesting early adaptations may resolve in the intermediate years after surgery to resemble similar patterns to control. The Late ACLR group demonstrated greater joint loading in the frontal plane, which may be exposing the joints to higher loads that play a role in long-term joint degeneration.

INTRODUCTION

Anterior cruciate ligament (ACL) tears result in significant knee joint instability and knee related disability. ACL reconstruction (ACLR) surgery in combination with post-surgical rehabilitation is a common treatment for physically active patients wishing to return to sport and exercise after ACL injury. Reports suggest that over 130,000 ACLR surgeries were performed annually in the United States in 2006, [1] and that the incidence rates continue to increase on an annual rate.[1] Currently, clinical care following ACLR is focused on the goal of a safe and timely return to sport and exercise. A recent study found that within 2-years post-surgery, 77% of ACLR patients had returned to some level of sport and only 47% had return to pre-injury sport.[2] For ACLR patients who do return to sport within 2-years post-surgery, evidence suggests that the incidence rate of a second ACL injury is nearly 6-times greater in those patients than healthy individuals without a history of ACLR.[3] While clinical care primarily focuses on the goal of a safe return to play, evidence suggests that long-term outcomes in ACLR patients are not favorable. Evidence suggests that patients with a history of ACLR are at a high risk for early onset post-traumatic osteoarthritis (PTOA).[4-6] A recent systematic review reported that within patients with a history of ACLR, 36% and 48% of patients had evidence of knee OA within first and second decades post-surgery, respectively.[4] This is particularly concerning when considering that the highest rates of ACLR are performed in patients under the age of 20.[1] Patients with a history of ACLR also self-report poorer knee-related function and lower physical activity levels than age-matched controls.[7]

Adaptations in lower extremity kinematics and kinetics following ACLR may contribute to the mechanical development of PTOA.[8] Unresolved post-traumatic impairments and limitations in proprioception, muscle function, and movement coordination may manifest into abnormal joint motion and loading during activities of daily living and exercise. Small deviations in normal knee joint mechanics may lead to altered wear patterns on the articular tissues of the

joint that over time and repetition could cause rapid or higher magnitude joint degeneration. Research has focused on identifying post-traumatic adaptations in lower extremity biomechanics, particularly joint kinetics, which may detrimental towards long-term joint health after ACLR.

Much of the ACL injury and ACLR literature has focused on gait adaptations about the knee during common repetitive activities such as walking, jogging, and stair ambulation, primarily in regards to sagittal plane kinematics and kinetics with more recent attention on frontal plane kinetics.[9] Gait adaptations are commonly evaluated by examine inter-limb differences in gait symmetry between ACLR and contralateral limbs or by comparing ACLR limbs to the limbs of healthy controls. [9] Reductions in external knee flexion moments during the stance phase of gait have been reported in patients after ACL injury and ACLR.[9,10] This 'quadriceps avoidance' gait pattern is considered an adaptation in response to quadriceps muscle dysfunction,[11] and evidence has shown that ACLR patients with weak quadriceps have demonstrated a reduced external knee flexion moment when compared to uninjured controls.[12] The external knee adduction moment has become a popular gait variable of interest in patients with a history of ACLR.[13-17] The role of the knee adduction moment in the development and progression of idiopathic knee osteoarthritis (OA) has been extensively studied.[18] The knee adduction moment is thought to represent greater medial knee joint loading,[19] leading to the higher rates of medial compartment tibiofemoral OA.[20] Evidence studying the presence and role of an altered knee adduction moment in ACLR knees has been conflicting.[9] Reports of significantly higher[14] and lower[15-17,21] knee adduction moments have been reported in patients with a history of ACLR compared to contralateral knees[15-17] and healthy controls knees.[14,21]A recent systematic review observed a trend in studies suggesting that walking knee adduction moment was lower in ACLR participants early post-surgery (~1-year) and higher in ACLR participants in later phases (5-years) post-surgery compared to healthy controls.[9]

Abnormal gait biomechanics after ACLR in combination with time and repetition is theorized to contribute to the development of PTOA. Early detection of potential deleterious gait patterns as they develop would allow clinicians the opportunity to intervene and potentially slow the development and progression of PTAO, however, there is limited understanding of when abnormal movement actually develop over the course of time post-surgery. The majority of ACLR gait research has studied either a group of ACLR patients at early time points post-surgery (6-12 months) or a lumped group of chronic ACLR patients that present over a wide distribution of times post-surgery. This limits the ability to discriminate potential changes in gait that may be occurring between the intermediate and late time-frames of ACLR chronicity. In addition, the few longitudinal studies that have been performed have maximal follow-up of 2-3 years post-surgery, [16,22] which may be too early to evaluate long-term adaptations post-surgery. Currently, it is unknown how gait adaptations present in patients at different time-frames after ACLR. Therefore, the purpose of this study was to compare walking and jogging knee and hip biomechanics in the sagittal and frontal planes between involved and uninvolved limbs in groups of ACLR patients at early, mid, and late time-frames post-surgery and healthy controls.

METHODS

Data collection was performed in a laboratory setting and included 3-dimentional motion capture of participants' gait during treadmill walking and jogging. Primary gait variables included sagittal and frontal knee and hip kinetics and kinematics and vertical ground reaction forces (vGRF). Gait variables were compared between the involved and uninvolved limbs within each group. The surgical knee limb and a randomly selected limb were treated as the involved limb in the ACLR and control participants, respectively. This study was approved by our University's institutional review board for health sciences research and all participants provided written informed consent.

Participants: A total of seventy-six individuals participated in this study. Fifty-six individuals had a history of primary, unilateral ACLR who were greater than 9-months post-surgery and had returned to exercise/sport with no physical activity restrictions imposed by their healthcare providers (Table I-1). ACLR participants were excluded if they had a history of multi-ligament knee surgery, surgical complications, or bilateral knee joint surgery. There were no restrictions on participation based on ACLR graft type or a history of meniscectomy or repair at the time of ACLR; however, participants with active meniscal symptoms (joint line pain, clicking) we not included. ACLR participants were stratified into Early ACLR (6-month to 2 years), Mid ACLR (2 to 5-years), and Late ACLR (5 to 15 years) groups based on their time post-surgery. Twenty recreationally active individuals with no history of lower extremity injury or surgery and no current symptoms of lower extremity pain or neuropathy participated as healthy controls (Table I-1). All participants were between the ages of 18-35 and were recruited from our local university community.

Data Collection: Demographic variables including age, sex, mass, height, and time post-surgery were collected and all participants completed the knee injury and osteoarthritis outcome score (KOOS),[23] the International Knee Documentation Committee (IKDC) subjective knee evaluation [24], and the Godin leisure-time activity [25] questionnaire to evaluated self-reported knee function and physical activity levels.

The motion capture system included Motion Monitor software (Innovative Sports Training, Inc., Chicago, IL), twelve Bonita10 cameras (Vicon Motion Systems, Ltd, UK) and a split-belt instrumented treadmill (Bertec Corporation, Columbus, OH). Retro-reflective markers (14mm) were placed bilaterally on the heel, 2nd toe, lateral malleoli, lateral shank, lateral knee joint, lateral thigh, anterolateral thigh, and anterior superior iliac spine (ASIS). A 4-marker sacral cluster was secured around the waist and aligned with the sacrum. An individual marker was placed on the dorsum of the right foot to distinguish from the left foot. Static calibration trials

were performed standing with feet shoulder-width apart and toes facing forward. Each body segment was defined using a minimum of 3 markers; Foot (heel, 2nd toe, lateral malleoli), shank (lateral malleoli, lateral shank, lateral knee joint), thigh (lateral knee joint, lateral thigh, anterolateral thigh), pelvis (ASISx2, sacral cluster). Ankle and knee joints were defined using the lateral malleoli and lateral knee joint markers and hip joint was defined using ASIS markers and the Bell method[26]. Participants performed trials in their preferred shoes used for jogging exercise. Walking and jogging trials were performed at standardized speeds of 1.34 m/s (3.0 mph) and 2.68 m/s (6.0 mph), respectively, with 5:00 minute warm-up periods for each task prior to collection. Ten capture periods of 3-seconds each were collected for each participant during walking and jogging.

Data Processing: Kinematic data were sampled at 100Hz, instrumented treadmill force data were sampled at 1000Hz, and all data were smoothed using a 20Hz Butterworth filter. Kinetic and kinematics variables were reduced to 100 data points representing 1-100% of the gait cycle (heel-contact to heel-contact). Variables were calculated using the average of 10 strides for each limb. For each capture period, the first full gait cycle (heel-contact to heel-contact) on the involved and uninvolved limb were selected using a threshold of 20N to define heel-contact. Vertical ground reaction forces (vGRF) were reported in Newtons normalized by body mass (N/kg), kinematics variables were reported in degrees, and kinetics were reported in external moments, Newton*meters (Nm) normalized by body mass and height (Nm/kg*m).

Statistical Analysis: Demographic data were compared between each group using one-way ANOVAs and Chi-squared analyses (sex, graft-type). Tukey's LSD *post-hoc* comparisons were performed when appropriate. Comparisons for graft-type and time post-surgery we only made between the three ACLR groups. Primary kinetics and kinematic variable comparisons were made between involved and uninvolved limbs within each group by graphically plotting the mean and 90% confidence intervals (CI) for each 1% of the gait cycle for each limb. Kinematic

variables were presented across 1-100% of the gait cycle. Kinetics variables were presented across the stance phase of gait, defined as 1-60% for walking and 1-40% jogging. Statistically significant differences between limbs were defined as regions of the gait cycle where the 90% CI did not overlap for a minimal of three consecutive percentages (3%) of the gait cycle.[27,28] The average magnitude of the difference (mean difference ± SD) and average Cohen's-d effect-sizes (ES)[29] and 95% CI (ES [95% CI]) were calculated for the region of the gait cycle where 90% CI did not overlap. Variables of interest were further explored by plotting the means of the involved limb and uninvolved limbs all four groups on the same graph for visual comparison. Data from two participants were not included in the jogging analyses: one participant from the Mid ACLR group (n=19) did not feel comfortable jogging and one from the Late ACLR group (n=17) had a collection error in the jogging data.

RESULTS

Figures I-1, I-2, I-3, and I-4 include inter-limb comparison graphs of gait variables of interest. Additional graphs are available for view in the appendices

Demographics: There were significant group differences in age (F=10.8, P<.001), KOOS (F=12.2, P<.001), and time post-surgery (F=94.1, P<.001). The Late group was significantly older than the Early ACLR (P<.001), Mid ACLR (P<.001), and Control (P<.001) groups (F=10.8, P<.001), but there were no differences in age between other groups (all P>.10). The Early ACLR (P<.001), Mid ACLR (P<.001), and Late ACLR (P<.001) groups all reported significantly lower KOOS (F=12.2, P<.001) and IKDC (F=14.1, P<.001) compared to the Control group. There were no differences in KOOS or IKDC scores between ACLR groups (all P>.09). Times post-surgery were significantly different between the Early, Mid, and Late ACLR groups (all P<.001). There was no significant differences in sex (X^2=1.8, P=.61), mass (F=.02, P=.99), height (F=.11, P=.95), or Godin score (F=1.69, P=.18) between the Early, Mid, Late

ACL, and Control groups. There was no significant difference in graft-type between the Early, Mid, and Late groups (X^2=5.1, P=.28).

Early ACLR Group: During walking, the Early ACLR group demonstrated greater knee flexion motion (47-59%, 4.0 ± .1 degrees, ES= 0.86 [.17, 1.54]) during terminal stance and greater hip abduction motion (82-95%, 2.1 ± .2 degrees, ES= 0.86 [.17, 1.54] during terminal swing on the involved limb compared to uninvolved limb (Figure I-1). During terminal stance of walking, the Early ACLR group demonstrated lower vGRF (52-56%, -0.80 ± .24 N/kg, ES= -0.95 [-1.63, -.26]), lower external knee extension moments (46-51%, -.09 ± .004 Nm/kg*m, ES= -0.98 [-1.67, -.28], and lower external knee adduction moments (52-58%, -.08 ± .02 Nm/kg*m, ES= -0.98 [-1.67, -.28]) on the involved limb compared to the uninvolved limb during terminal stance (Figure I-1). There were no significant differences between limbs in sagittal hip kinematics or kinetics, frontal knee kinematics, or frontal hip kinetics during walking.

During jogging, the Early ACLR group demonstrated less knee flexion motion (19-21%, -4.0 ± .1 degrees, ES= -0.85 [-1.54,-.17]) during mid-stance and less hip adduction motion (86-96%, -2.6 ± 0.2 degrees, ES= -0.87 [-1.55, -.18]) during terminal swing on the involved limb compared to uninvolved (Figure I-2). During jogging stance, the Early ACLR group demonstrated lower vGRF (19-24%, -1.38 ± .10 Nm/kg, ES= -1.10 [-1.80, -.40], lower external knee flexion moments (10-20%, -0.26 ± .03 Nm/kg*m, ES= -0.91 [-1.59, -0.22]), lower external knee adduction moments (23-25%, -0.20 ± .01 Nm/kg*m, ES= -0.92 [-1.61, -.23], and lower external hip adduction moments (23-25%, -0.29 ± .02 Nm/kg*m, ES= -0.85 [-1.53, -.17] on the involved limb compared to the uninvolved limb (Figure I-2). There were no differences between limbs in sagittal hip kinematics and kinetics, frontal knee kinematics and frontal hip kinetics during jogging.

Mid ACLR Group: There were no significant differences in walking or jogging kinetic or kinematic variables between the involved and uninvolved limbs in the Mid ACLR group.

Late ACLR Group: During the stance phase of walking, the Late ACLR group demonstrated a greater external knee adduction moments (16-32%, 0.09 ± .02 Nm/kg*m, ES= 0.87 [.19, 1.56] and a greater external hip adduction moments (10-58%, 0.18 ± .03 Nm/kg*m, ES= 1.13 [.43,1.84]) on the involved limb compared to the uninvolved limb (Figure I-3). There were no significant differences between limbs in vGRF, sagittal knee or hip kinematics or kinetics, or frontal knee or hip kinematics.

During the stance phase of jogging, the Late ACLR group demonstrated greater external hip adduction moments (7-9, 13-16, 20-23, 27-30%, 0.38 ± .14 Nm/kg*m, ES= 1.01 [.29, 1.72] on the involved limb compared to the uninvolved limb (Figure I-4). There were no significant differences between limbs in vGRF, sagittal knee and hip kinematics and kinetics, frontal knee kinetics and kinematics, and frontal hip kinematics.

Control Group: There were no significant differences in walking or jogging kinetic or kinematics variables between the involved and uninvolved limbs in the Control group.

External Knee Adduction Moment in All Groups: We chose to visually inspect plots of the involved and uninvolved limb external knee adduction moments for all four groups during walking and jogging (Figure I-5). On the involved limb, we observed a potential pattern that may suggest the external knee adduction moment was lowest in the Early ACLR group, greater in the Mid ACLR group, and greatest in the Late ACLR group. On in the uninvolved limb, we observed a potential pattern in the opposite direction that may suggest external knee adduction moment was lowest in the Late group and greater in the Mid and Early ACLR groups.

DISCUSSION

The purpose of this study was to evaluate inter-limb differences in walking and jogging knee and hip kinetics and kinematics in ACLR patients at Early, Mid, and Late time-frames post-surgery and healthy controls. Gait asymmetries were only observed in the Early and Late ACLR groups. The Early ACLR group demonstrated the most walking and jogging gait asymmetries, with inter-limb differences in vGRF, and knee and hip kinetics and kinematics in the sagittal and frontal planes . The Late ACLR group only demonstrated inter-limb differences in frontal plane kinetics at the knee and hip during walking and jogging. All inter-limb differences in gait were not only statistically different, but were also supported by large magnitude effect-sizes (>0.80) with 95% confidence intervals that did not cross zero, suggesting meaningful inter-limb differences. [29] Both the Mid ACLR and Control groups did not demonstrate inter-limb differences in walking or jogging gait variables, suggesting that gait may be most symmetrical during the intermediate time frame after ACLR surgery and more similar to normal gait patterns of healthy controls.

Early ACLR: The Early ACLR group was the only group to demonstrate inter-limb differences in the sagittal plane and vGRF. During walking, the Early ACLR group demonstrated average of 4-degrees greater knee flexion on the involved limb during terminal stance when peak knee extension normally occurs; suggesting ACLR subjects were avoiding full knee extension. Knee extension avoidance may be early protective adaptation to spare the ACL graft from anterior translation of the tibia on the femur during terminal knee extension,[30] or a lack of quadriceps contraction during the propulsive phase of terminal stance. This period of knee extension avoidance also coincided with the lower external knee extension moment, lower vGRF, and lower external knee adduction moment on the involved limb during terminal stance. These findings are consistent with previous studies that have observed reduced peak knee extension moments in ACLR limbs averaging 9 to 26-months[17,31] post-surgery when compared to

contralateral[17] and control[31] knees, and reduced peak knee adduction moments in ACLR limbs averaging 10-26-months[15-17] post-surgery compared to contralateral knees.[15-17]

In the Early ACLR group, walking gait asymmetries were all observed during the terminal stance phase of gait, which includes the period of double-limb support in which the involved limbed is moving towards toe-off and the uninvolved limb has initiated heel contact. The reductions in joint moments and vGRF on the involved limb of the Early ACLR group may suggest a protective adaptation in walking gait early after ACLR to avoid joint loading on the involved knee. This pattern to limit joint loading may serve the purpose of protecting the joint and reducing the strain on impaired muscles, such as the quadriceps, [32-34] that are normally used to attenuate joint loads. Reducing joint loads may be achieved during this phase of double-limb support by transitioning body mass support anterolateral towards the uninvolved limb, thus reducing joint loading sooner on the involved knee. We also observed a difference in hip abduction between limbs during terminal swing (82-95%). Since terminal stance on one limb corresponds with terminal swing on the other limb, we suspect that the difference in terminal swing is most likely an a reduction in hip abduction in the uninvolved limb as it prepares for heel contact that is occurring in conjunction to the adaptations in the involved limb during terminal stance.

During jogging, asymmetries in the Early ACLR group were primarily observed during mid-stance of the gait cycle. Contrary to walking, we did observe the commonly described reduction in knee flexion motion and moment that is thought to suggest a pattern of “quadriceps avoidance”. [10,11] The higher forces associated with jogging may explain the presences of quadriceps avoidance pattern during jogging but not walking in the Early group. We also observed reductions in vGRF and knee and hip adduction moments in the involved limb compared to the uninvolved, suggesting a similar protective pattern of joint loading avoidance on the involved ACLR limb that was observed during walking. Unlike walking, the entire stance

phase of jogging occurs during single-limb support. Participants may be using forward and lateral trunk leaning, towards the injured knee, to reduce the magnitude of knee flexion and adduction loading on the involved knee.[35] Patient early after ACLR (7.4 ± 1.5 months) have demonstrated greater forward and lateral trunk lean towards the ACLR limb and reduced external knee flexion moments while jogging when compared to healthy controls.[35] Jogging is commonly recommended by clinicians for patients in the early stages after ACLR as "safe" exercise activity; however, there is limited evidence describing jogging biomechanics in individuals early after ACLR.[9]

Mid ACLR: The Mid ACLR group did not demonstrate significant inter-limb differences in any of the gait variables examined in this study. These findings were similar to what was observed in the control group, which may suggest that ACLR participants in this mid time-frame, 2-5 years post-surgery, may be demonstrating more "normal" gait patterns. We observed numerous inter-limb differences in the Early ACLR group that were not present in the Mid ACLR group, suggesting a potential role of time post-surgery in gait biomechanics. As patients are further in time from the trauma of surgery and matriculate back into normal physical activity, adaptations in gait biomechanics may begin to normalize.

Late ACLR: The Late ACLR group only demonstrated frontal plane gait asymmetries which manifested as greater knee and hip adduction moments in the involved limb during walking and a greater hip adduction moment during jogging. During jogging, there was a trend towards greater knee adduction moment across the entire gait cycle; however there was no region that reached a statistically significant difference for 3 consecutive percentage points of the gait cycle. Previous reports have identified increased peak knee adduction moments during walking in ACLR knees later (5.3 years) post-surgery compared to controls,[14] while others have observed a trend towards a greater knee adduction moment in patients later post-surgery (6-years).[36] During both walking and jogging, the plots of knee and hip adduction moments suggest that the Late

ACLR group was demonstrating increased adduction moments in the involved limb and potentially a decrease in adduction moments in the uninvolved limbs. Since we did not observed inter-limb difference in knee and hip kinematics, we theorized that frontal plane adaptations in knee and hip kinetics may be the result of medial-lateral shifts in the line of action of the vGRF that alters the joint moment arm.[37] Shifting the line of the vGRF away from the stance limb would increase the adduction moment, while shifting away from the stance limb would decrease the adduction moment. One strategy that participants in the Late ACLR group may be using is a shift in lateral trunk lean. Evidence has shown that lateral trunk lean is a significant predictor of knee adduction moment in individuals with knee OA.[38] To the patient, this may seem like a beneficial adaptation to shift their mass away from their ACLR knee; however, this shift may cause focal joint loading in that medial compartment of the knee that over time and repetition leads to aggressive wear and tear of the tissues. Unfortunately, we did not collect trunk data so we do not have the data to substantiate this theory. Adaptation quadriceps and lateral hip musculature may also play a role in the presentation of these gait patterns in the Late group.

Temporal Gait Adaptations: The presence of an increase knee adduction moment in only the Late ACLR group is an interesting finding in context of the theoretical relationship between increased knee adduction moment, increased medial knee joint loading, and the development of knee OA.[19] If this potentially detrimental gait pattern develops years after ACLR, then clinical care and research efforts could benefit from including serial follow-ups of ACLR patients to track and treat progressive changes in movement patterns and muscle function that develop over the course of ACLR chronicity. Interestingly, we observed opposite knee and hip adduction patterns in the Early and Late ACLR groups and no frontal plane asymmetries in the Mid ACLR group. These observations, in combination with the pattern observed when visualizing the external knee adduction moment means of all four groups, may suggest a temporal shift in walking and jogging gait strategies across ACLR chronicity. Early post-surgery when

patients are adjusting back to sport/exercise, patients may be adapting a protective strategy that reduces frontal and sagittal knee joint loading during walking and jogging. In the mid time-frame, when patients have fully matriculated back into physical activity and joint protection may no longer be necessary or no longer a conscious practice, gait patterns may begin to normalize. This may be supported by the pattern observed in the involved limb graphs of Figure I-5 which suggest joint loading may increase in the Mid group compared to the Early group. Over time in the later time-frame post-surgery, patients may develop faulty movement patterns potentially in response to prolonged muscle dysfunction which exploits the knee to elevated adduction loading patterns that are potentially dangerous to long-term joint health. Future long-term longitudinal gait analysis research is warranted to better understand potential temporal changes in movement strategies and joint loading in patients with a history of ACLR.

Limitations: This study is not without limitations. We studied the role of time using a cross-sectional design rather than longitudinal. We stratified ACLR participants based on clinically relevant time points: <2-years being the time-frame most patients are returning to sport[2] and at are highest risk of suffering a secondary ACL injury[3], 2-5 years being a time-frame ACLR patients are few years removed from ACLR but probably still continuing sport and higher level exercise, and 5-15 years being a long-term time-frame post-surgery but theoretically before major joint degeneration is occurring. We made the decision to perform primary analyses as inter-limb comparisons within each group and did not examine direct statistical comparisons between each group. While this limits our ability to make direct inferences between groups, we felt this analysis allowed for better control of inherent variability between participants by looking at adaptations in the ACLR limb as they relate to participants contralateral, uninvolved limb. We did not have radiographic exams to definitively know that participants in this study were not already developing signs of knee OA. This makes it particularly difficult to theorize whether gait adaptations observed the Late group are a precursor to or a product of developing knee OA. We

attempted to maintain homogeneity of demographics between ACLR groups outside of the time post-surgery variable; however, the Late ACLR group was significantly older than the other groups. The Late group was still relatively young, average age 26.7 years, but age in combination with time post-surgery may play a role in the differences observed in the Late ACLR group.

CONCLUSIONS

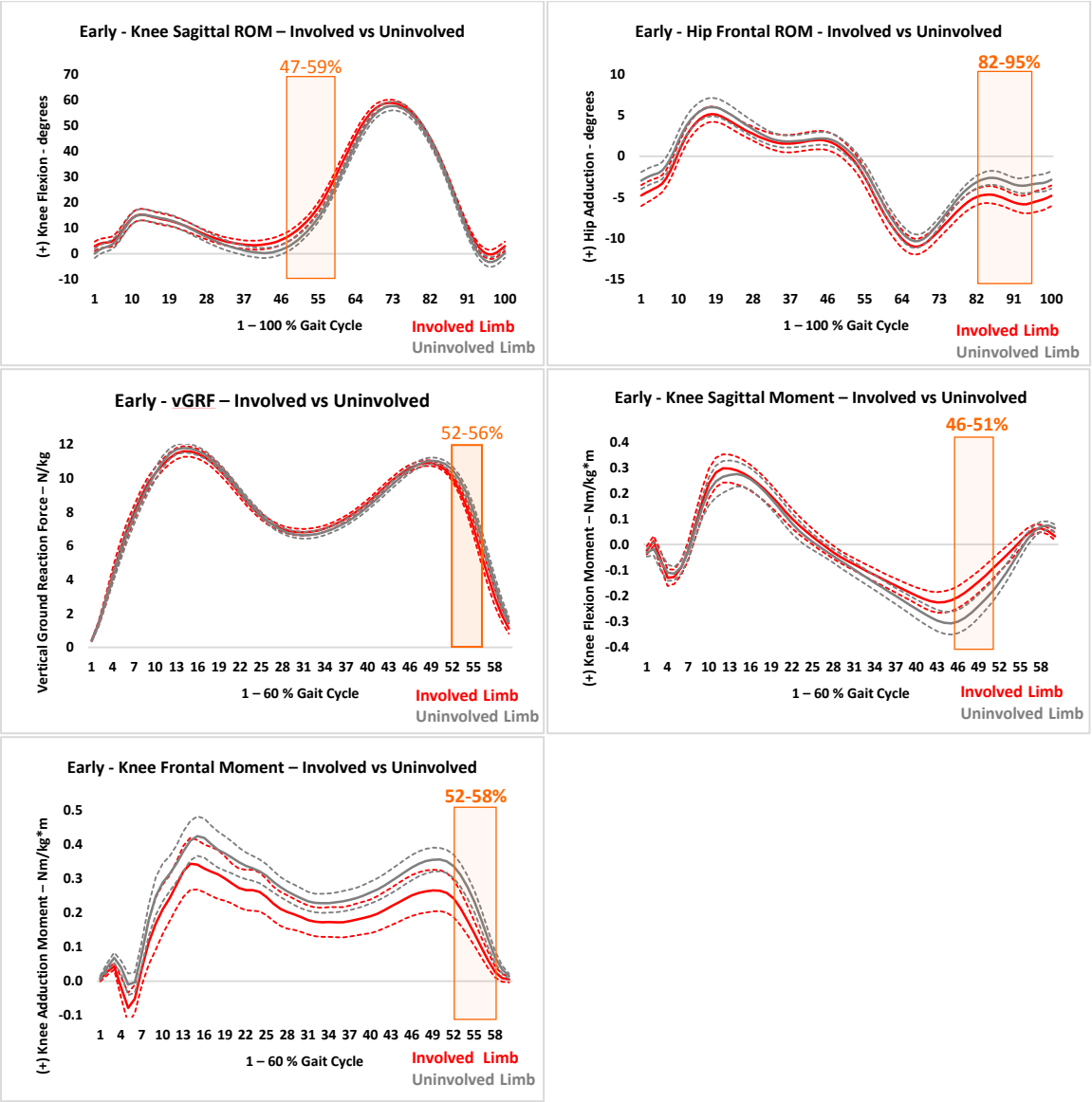
Temporal changes in gait biomechanics may occur over the course of ACLR chronicity. Walking and jogging gait adaptations were most prevalent in the Early and Late ACLR groups. There were no significant gait asymmetries in the Mid ACLR and Control groups. Early ACLR group walked and jogged with lower sagittal and frontal knee and frontal hip loading on their involved limb, potentially to protect the knee during the early time-frame post-surgery. The Late ACLR group walked and jogged with greater frontal knee and hip loading on their involved limb. A shift in frontal plane joint loading may occur over the course of ACLR chronicity from a pattern that protects the knee joint early to a pattern that may expose the knee joint to increased loading later after ACLR.

Table I-1. Early ACLR, Mid ACLR, Late ACLR and Control Group Demographics

	Early ACLR (n = 18)	**Mid ACLR (n = 20)**	**Late ACLR (n = 18)**	**Control (n = 20)**
Sex $_{F,M}$	11 F, 7 M	16 F, 4 M	12 F, 6 M	13 F, 7 M
Age $_{years}$	21.7 ± 4.1	20.5 ± 2.2	26.7 ± 4.4 [a]	22.4 ± 3.2
Mass $_{kg}$	68.7 ± 15.6	68.5 ± 9.9	69.5 ± 12.7	68.9 ± 13.1
Height $_{m}$	1.72 ± .12	1.73 ± .09	1.73 ± .10	1.71 ± .13
KOOS $_{0\text{-}100}$	88.8 ± 6.9 [b]	90.7 ± 5.5 [b]	92.1 ± 7.2 [b]	99.3 ± 1.8
IKDC $_{0\text{-}100}$	85.4 ± 9.2 [b]	86.0 ± 7.2 [b]	89.8 ± 10.1 [b]	99.5 ± 2.0
Godin	69.2 ± 22.8	74.5 ± 13.0	59.9 ± 26.4	70.5 ± 17.9
Time Post-Surgery, $_{months}$	17.1 ± 5.3 [c]	39.4 ± 7.7 [c]	102.7 ± 33.0 [c]	NA
Graft-Type	Patella tendon - 7 Hamstrings - 10 Cadaver - 1	Patella tendon - 11 Hamstrings - 5 Cadaver - 4	Patella tendon - 10 Hamstrings - 5 Cadaver - 3	NA

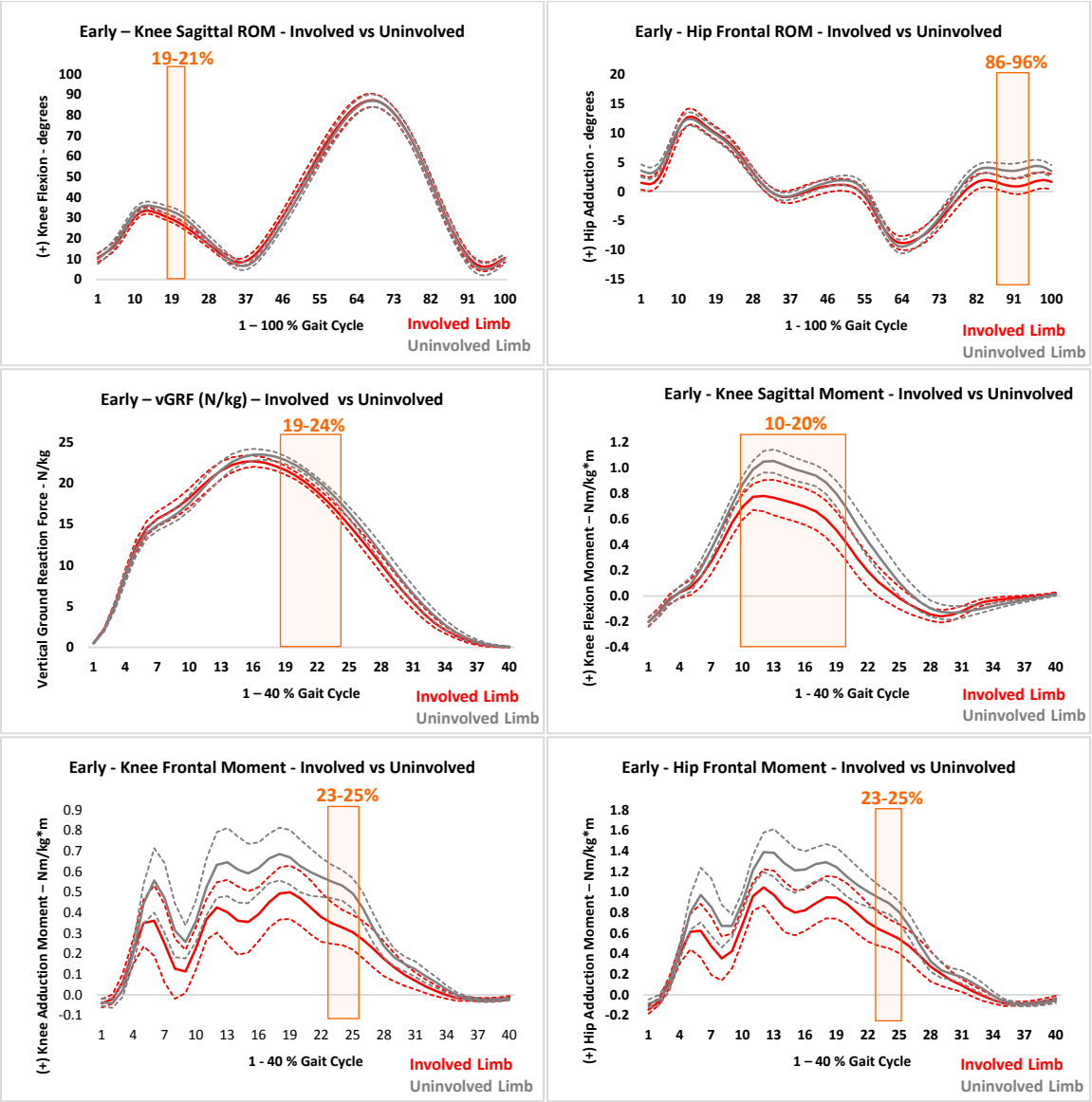
[a] Significantly greater than all other groups (P<.001)
[b] Significantly lower than control group (P<.001)
[c] Significantly different from other ACLR groups
P-value = One-way ANOVA test or Chi-Squared test (sex, graft)

Figure I-1. Walking, Early ACLR Group: Means and 90% Confidence Intervals of Kinematic and Kinetics Variables for Involved and Uninvolved Limbs



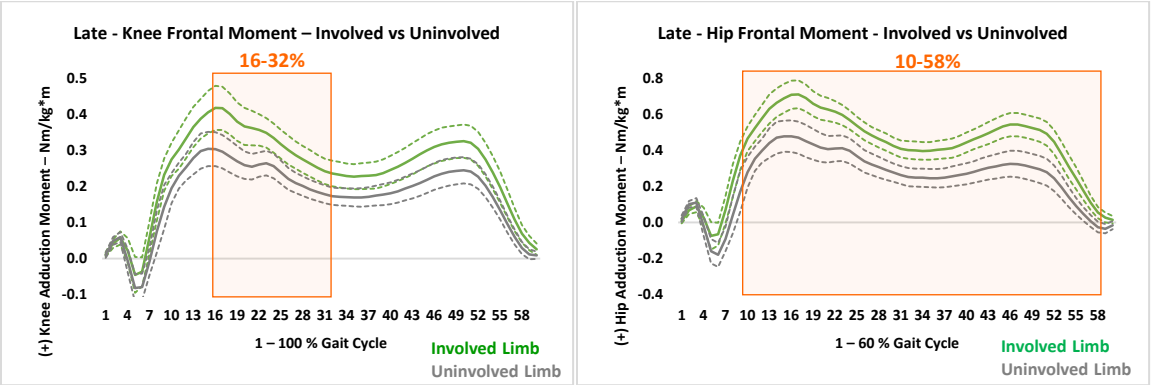
Solid line = limb mean, dashed line = 90% confidence interval upper and lower bounds, Orange box = region where 90% confidence intervals do not overlap

Figure I-2. Jogging, Early ACLR Group: Means and 90% Confidence Intervals of Kinematic and Kinetics Variables for Involved and Uninvolved Limbs



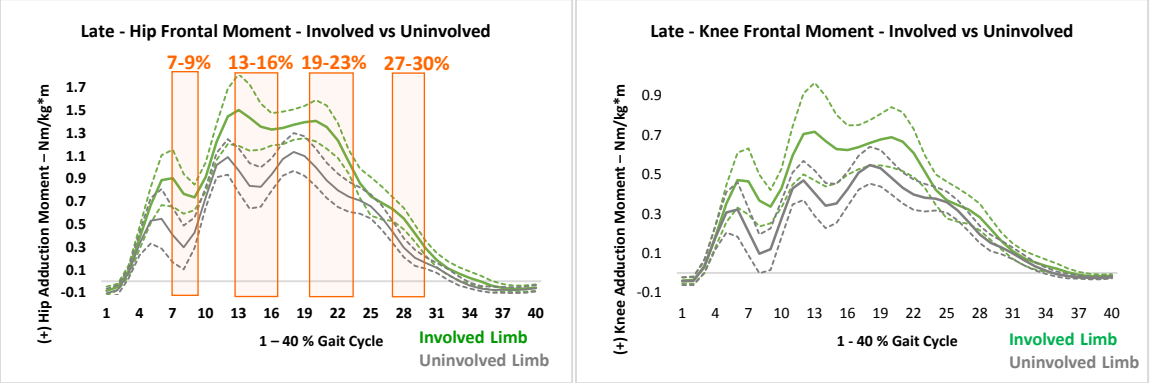
Solid line = limb mean, dashed line = 90% confidence interval upper and lower bounds, Orange box = region where 90% confidence intervals do not overlap

Figure I-3. Walking, Late ACLR Group: Means and 90% Confidence Intervals of Kinetics Variables for Involved and Uninvolved Limbs



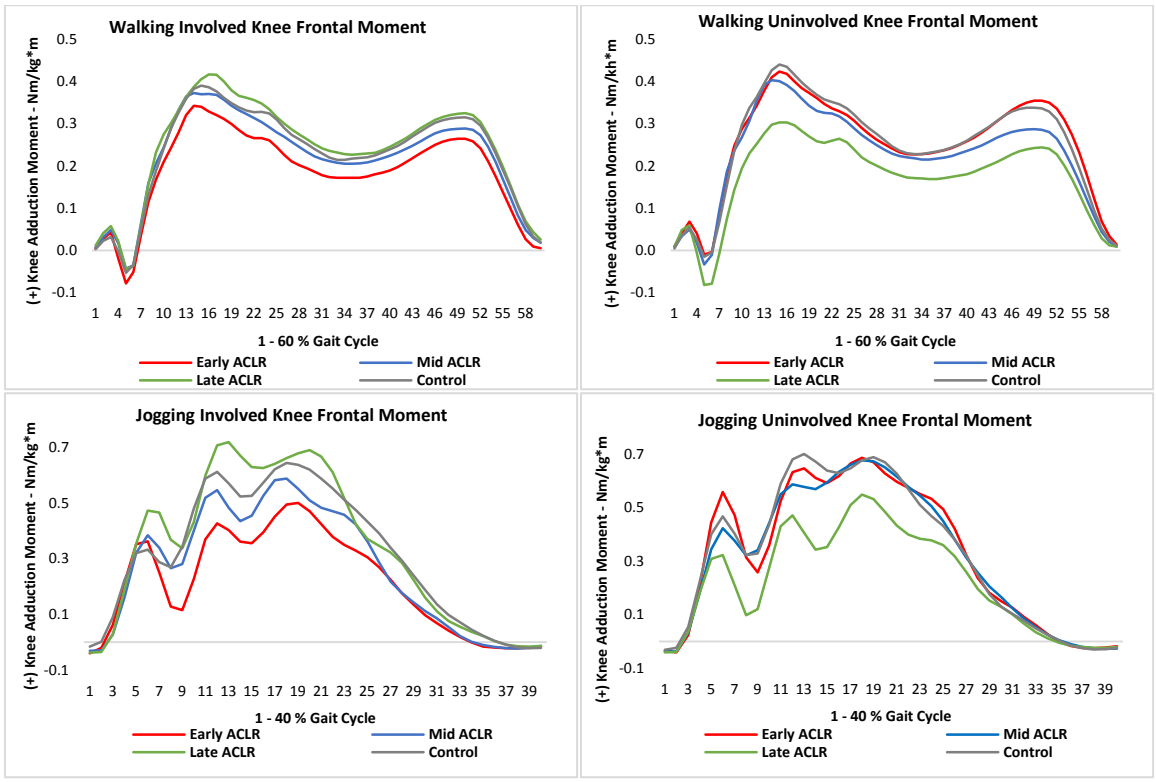
Solid line = limb mean, dashed line = 90% confidence interval upper and lower bounds, Orange box = region where 90% confidence intervals do not overlap

Figure I-4. Jogging, Late ACLR Group: Means and 90% Confidence Intervals of Kinetics Variables for Involved and Uninvolved Limbs



Solid line = limb mean, dashed line = 90% confidence interval upper and lower bounds, Orange box = region where 90% confidence intervals do not overlap

Figure I-5. Walking and Jogging, All Groups: Mean Frontal Plane Knee Kinetics in the Early, Mid, Late ACLR, and Control groups' Involved and Uninvolved Limbs



SECTION II: MANUSCRIPT II

SUBMAXIMAL QUADRICEPS FORCE CONTROL DURING ISOMETRIC, CONCENTRIC, AND ECCENTRIC FORCE-MATCHING TASKS IN ACL RECONSTRUCTED KNEES

ABSTRACT

Background: Quadriceps muscle dysfunction has been associated with poor knee function and altered movement patterns in individuals with a history of anterior cruciate ligament reconstruction. Quadriceps force control is a measure of muscle function that may provide unique information regarding muscle contraction variability and accuracy, and greater force variability has been associated with poor ACL knee function. ACLR knees have shown altered quadriceps force control during maximal contractions; however, there is limited study of force control during submaximal contractions that are more common during daily activities. **Methods:** Fifty-seven ACLR knees and 20 healthy knees performed isometric, concentric, and eccentric quadriceps force-matching tasks at a target contraction of 25% of maximum contraction. Force standard deviation (SD), force coefficient of variation (CV), and force root mean square error (RMSE) we calculated during force-matching task for each contraction type. Force control variables were compared between ACLR and controls using independent t-tests and Cohen's-d effect sizes. Association between force control variables and time post-surgery, subjective knee function, and physical activity levels were made using Pearson's r correlation coefficients. **Results:** The ACLR group demonstrated lower force SD and RMSE during concentric and eccentric force matching tasks (all $P<.05$). There were no differences between groups during isometric force matching tasks. There were no associations between measures of force control and time post-surgery or subjective knee function. Lower SD ($r= .28$, $P<.05$) and error ($r= .36$, $P<.05$) during concentric contractions were correlated with lower levels of physical activity in ACLR participants. **Conclusions:** ACLR knees may demonstrate lower quadriceps force variability and error during submaximal contractions, which is contrary to previous evidence suggesting ACLR knee demonstrate higher quadriceps force variability during maximal contractions. Lower force variability and error may reflect adaptations in neuromuscular function that present in individuals with lower physical activity levels.

INTRODUCTION

The primary treatment option for physically active individuals who suffer an anterior cruciate ligament (ACL) tear is surgical ACL reconstruction (ACLR). An estimated 130,000 ACLR surgeries are performed each year in the United States and evidence shows that incidence rates continue to increase each year.[39] While traditionally the primary goal of ACLR is to allow patients to return back to sport and exercise, evidence suggest that a large proportion of patients are unable to return to sport,[40] and go on to experience long-term limitations in knee function that can impede their ability to be physically active and perform activities of daily living.[5,41] Additionally, patients with history of ACLR have a high risk of experiencing early-onset knee osteoarthritis (OA), leading to further functional disability.[4,5]

Quadriceps muscle dysfunction is a common, immediate, and persistent clinical concern following ACLR.[32-34] The quadriceps muscles play a key role in knee joint function and health as a primary muscle group for knee motion, dynamic knee joint stability, and force attenuation at the knee during lower extremity loading. Deficits in quadriceps strength and force control have been associated with poorer subjective knee function in chronic ACLR patients that are years post-surgery. [42,43] Additionally, ACLR patients with weak quadriceps have demonstrated altered knee joint loading during gait,[12] which researchers suspect may be a predisposing factor towards the initiation and progression of rapid joint degeneration.[8] Despite targeted rehabilitation post-surgery, there is extensive evidence indicating impairments in quadriceps muscle function are a persistent problem for years after surgery.[27,32,33,44] Chronic ACLR patients have demonstrated quadriceps muscle impairments in various aspects of muscle function, including force control[42,44-46], strength[27,32,33], and activation[27,32]. Researchers theorize that long-term deficits in quadriceps muscle function is a consequence of neural adaptations at the time of injury and surgery, which alter proprioceptive input from peripheral sensory receptors and inhibit neuromuscular activation of quadriceps muscle fibers.[34,47] Currently, there is limited understanding of the natural development and progression of quadriceps muscle dysfunction over time after ACLR.

Quadriceps muscle force control refers to the ability to produce a steady and accurate muscle contraction during static or dynamic contraction tasks.[48] Quadriceps force control has been studied a variety of knee pathologies including ACLR, [42,44,45] ACL deficiency, [49] knee OA[50-52], and experimental knee pain.[53] Impairments in quadriceps force control, quantified as greater variability in the force output, have been observed in ACLR knees compared to healthy control knees,[42,44-46] and impaired quadriceps force control has shown to predict poorer subjective knee function in patients with a history of ACLR.[42] While several studies have used maximal knee extension contractions, isokinetic concentric[45] and isometric, [42,44] to gain insight into the quadriceps force control following ACLR, maximal quadriceps muscle contractions are not common during normal daily and physical activities. Therefore, understanding the effects of ACLR on submaximal quadriceps muscle control may provide greater insight into how ACLR impacts daily quadriceps muscle and knee function.

Submaximal quadriceps force control has been studied in knee OA patients, [50-52,54] with participants performing force-matching tasks in which they attempt to match and hold a knee extension contraction at a submaximal target force. Force control is commonly quantified using measures of variability, force standard deviation (SD)[50-52] or coefficient of variation[42,44,50], and measures of matching error between contraction forces and the matching target force[46,52,55]. In knee OA studies, submaximal force matching tasks have been performed during isometric[51,52] and isokinetic concentric and eccentric [50,52] contraction types. Greater force SD and error have been observed during submaximal concentric and eccentric contractions in OA knees compared to healthy controls, and impaired force control was associated with poorer functional outcomes.[52]

Evidence suggests that ACLR patients are at a greater risk of developing knee OA and chronic knee disability and that the development of long-term adaptation in quadriceps muscle function may play a role in the progression of poor outcomes after ACLR. Quadriceps force control, specifically at submaximal intensities, may be a valuable determinant of muscular

performance that more closely relates to quadriceps contractions that are utilized during daily functional tasks such as walking. Therefore, the primary aim of this study was to compare measures of submaximal force control steadiness and accuracy between patients with a history of ACLR and healthy controls. Our secondary aim was to examine the role that time post-surgery plays in quadriceps force control. We hypothesized that participants with a history of ACLR would demonstrate greater force standard deviation and error during submaximal force matching tasks compared to healthy controls, and that ACLR participants later post-surgery would demonstrate the greatest force standard deviation and error compared to other ACLR groups and healthy controls.

METHODS

This was a controlled laboratory study in which each participant completed submaximal isometric, concentric and eccentric[50,52,53] force-matching tasks at submaximal force of 25% of the participants' maximum isometric contraction (MVIC). The independent variables were groups, ACLR and control groups and Early ACLR, Mid ACLR, and Late ACLR groups. The dependent variables included force standard deviation, coefficient of variation, and root mean square error during isometric, concentric, and eccentric force matching tasks. The surgical limb of ACLR participants and a randomly selected limb of healthy controls were selected as the test limb for all tasks. Prior to testing, all participants completed a 5-minute cycling warm-up and all force-matching testing procedures were first performed on the participant's non-test limb to allow for substantial familiarization and practice of the testing procedures without fatiguing the test limb. This study was approved by our university's institutional review board for health sciences research and all participants provided written informed consent.

Participants: A total of seventy-seven individuals volunteered for participation in this study. Fifty-seven individuals with a history of primary, unilateral ACLR and twenty healthy controls were recruited from the local university community (Table II-1). All participants were between the ages of 18-35 years, with no history of lower extremity injury in the previous 6-

months. ACLR participants were greater than 6-months post-surgery and had returned back to normal physical activity with no restrictions from a health care provider. ACLR participants with a history of multi-ligament reconstruction, surgical complications, or bilateral knee joint surgery were excluded. History of meniscectomy or meniscal repair on the ACLR knee was not an exclusion criterion as long as the patient did not present with clinical signs or symptoms of continued meniscal pathology. For the secondary aim of the study, the ACLR participants were stratified by time post-surgery into Early ACLR, 9-months to 2-years (n= 19), Mid ACLR, 2-years to 5-years (n= 20), and Late ACLR, 5-years to 15 years (n = 18), groups. Twenty recreationally active healthy controls with no history of lower extremity pathology or injury, no current symptoms of lower extremity pain or neuropathy also participated. All participants completed the Knee Injury and Osteoarthritis Outcome Score (KOOS),[23] the International Knee Documentation Committee subjective knee evaluation form,[24] and the Godin Leisure-Time Activity scale (Godin)[25] to evaluate participants perceived knee-related function and regular physical activity participation.

Maximum Voluntary Isometric Contraction (MVIC): Target forces for matching tasks were determined by first establishing each participant's knee extension MVIC at 45°.[50] Patients were seated in a Biodex System III dynamometer (Biodex Medical Systems, Inc., Shirley, NY) with back flat against the chair, hips flexed to 80°, arms across the chest, the axis of rotation aligned with knee joint center, and the lever arm secured just superior to the malleoli of the test limb. Patients performed a series of progressive warm-up knee extension contractions, followed by three MVIC trials. Participants were instructed to gradually increase their contraction until maximum and hold steady for 3-seconds. A 1.5-second epoch during the maximum trial was used to calculate knee extension MVIC. Mass normalized MVIC (Nm/kg) was also calculated for analyses.

Force-Matching Tasks: Participants remained in the Biodex dynamometer for force-matching tasks. For all force-matching trials, target forces were displayed as a bold horizontal

line across the screen and participants were instructed to match a moving line representing their force output to the target force line as steady and accurate as possible. Visual feedback for force-matching was provided via a 110-cm television screen positioned approximately 1.5-meters in front of the participant. Force visual feedback was displayed as a percentage of participants' MVIC and the y-axis was set at 0-60% MVIC to standardized visual feedback across participants. Isometric force-matching tasks were performed at 45° knee flexion[50] and target contractions of 25% of the participants MVIC. For each trial, the participant matched the target force line and held the contraction for 5-seconds. Five trials were performed with rest between trials. The first two trials were treated as practice and the last 3 trials for each target were used for analyses. Concentric and eccentric force-matching tasks were performed at a target contraction of 25% MVIC and speed of 10°/second.[53] Each trial included a concentric contraction, in which the knee was extended from 65-15° and an eccentric contraction, in which the knee was flexed from 15-65°, for total knee range of motion of 50° for both contraction types. A total of twelve trials, alternating between concentric then eccentric contractions, were performed with 1-minute of rest every four trials to limit fatigue. The first nine trials were treated as practice and the final three concentric and eccentric trials were used for analyses. Knee joint range of motion was simultaneously recorded from the dynamometer for processing purposes.

Data Processing: Force data were digitized at 125Hz, smoothed using a 10-sample moving median filter, and processed using AcqKnowledge 4.2 software (Biopac System, Inc., Goleta, CA). For isometric trials, data were analyzed from the middle 3-seconds of the 5-second contraction and averaged for the three test trials. For the isokinetic concentric and eccentric trials, data were analyzed from the central 30° of the 50° range of the contraction and averaged for the three test trials. Force standard deviation (SD) and coefficient of variation (CV = SD of force/mean of force × 100) were calculated. Additionally, the error between the contraction force and target force for all data points was calculated using the root mean square error (RMSE).[46,53]

Statistical Analyses: Comparisons of demographic variables between ACLR and control participants were performed using independent samples t-tests continuous data and a chi-squared test for categorical data. Comparisons of MVIC, normalized MVIC, and force-matching variables (SD, CV, RMSE) between ACLR and control participants were performed using independent sample t-tests and calculations of Cohen's-d effect sizes and 95% confidence intervals. Effect sizes point estimates were interpreted as <0.2 = minimal, ≥ 0.2 = small, ≥ 0.5 moderate, ≥ 0.8 = large.[29] Effect- sizes with 95% confidence intervals not-including zero were interpreted as indicating a clinically important effect. Force matching variables that were significantly different between ACLR and control groups were further examined by calculating Pearson's correlation coefficients between force matching variables and four variables of interest: time post-surgery, normalized MVIC, KOOS, IKDC, and Godin. Correlation coefficients were interpreted as weak = 0 to 0.4, moderate 0.4 to 0.7, and strong = 0.7 to 1.0.[43]

The secondary aim included one-way ANOVAs with *post-hoc* fisher LSD to compare MVIC, and force matching variables (SD, CV, and RMSE) between Early, Mid, and Late ACLR groups and the control group. Variables that did not meet the criteria for parametric statistics were analyzed using Kruskal-Wallis tests. All statistical analysis were run using SPSS Statistics, version 23 (IBM Corporation, Armonk, NY) and statistical significance was set at $P < 0.05$ for all analyses.

RESULTS

ACLR vs Control: ACLR participants reported poorer knee function on the KOOS compared to healthy controls (Table II-1). There were no differences in sex, age, mass, height, or Godin score between ACLR and control groups (Table II-1). The ACLR group demonstrated significantly lower force SD and RMSE during concentric contractions, lower force SD during eccentric contractions, and lower normalized MVIC compared to control group (Table II-2). Group differences were supported by moderate to large effect sizes with 95% confidence

intervals that did not cross zero (Table II). There were no group differences for all other force control variables (Table II).

Time Post-surgery and Force Control: Means and standard deviations for MVIC and force control variables in each time post-surgery subgroup and controls are displayed in table II-3. Concentric force SD was significantly lower in the Early ACLR (P=.02), Mid ACLR (P=.05), and Late ACLR (P=.01) groups compared to control group (F=3.2, P=.03). There were no significant differences in concentric force SD between the three ACLR groups (all P>.42).

Concentric force RMSE was significantly lower in the Early ACLR (P=.01), Mid ACLR (P=.04), and Late ACLR (P=.05) groups compared to control group (F=2.7, P=.05). There were no significant differences in concentric force RMSE between the three ACLR groups (all P>.54). There were no significant differences between groups for normalized MVIC (F=2.2, P=.10), or the additional isometric (SD: F=1.2, P=.33, CV: F=0.9, P=.47, RMSE: χ^2= 4.8, P=.19), concentric (CV: F=0.9, P=.43) or eccentric (SD: χ^2= 4.8, P=.19, CV: F=0.3, P=.82, RMSE: F=1.5, P=.23) force control variables.

Correlations: Concentric force SD and RMSE exhibited positive, weak-to-moderate correlations with normalized MVIC and Godin score in ACLR participants (Table II-4), suggesting lower normalized MVIC and lower physical activity levels were correlated with lower force SD and error. Eccentric force RMSE was not correlated with normalized MVIC or Godin Score (Table II-4). Concentric force SD and RMSE and eccentric force RMSE were not correlated with time post-surgery, KOOS, and IKDC (Table II-4).

DISCUSSION

Based on previous evidence showing impaired maximal quadriceps force control in ACLR knees compared to healthy controls, we hypothesized that during submaximal contractions patients with a history of ACLR would also demonstrate greater force SD and error during submaximal force matching tasks. Contrary to our hypothesis, ACLR participants demonstrated lower force SD and RMSE during submaximal concentric and eccentric contractions when

compared to healthy controls. For all other force control measures, there were no differences between the ACLR and control participants. ACLR participants also demonstrated weak quadriceps as evidenced by the lower normalized MVIC. These findings suggest patients with a history of ACLR demonstrate weaker quadriceps muscles and may develop adaptations in neuromuscular function that present as decreased variability and error in submaximal force matching tasks.

Only one previous study has examined submaximal force control in ACLR knees. That study reported greater force error (RMSE) in ACLR knees compared to healthy controls.[46] Our contradictory findings may be due to differences in force-matching task contraction types and procedures. We observed differences in ACLR knees during concentric and eccentric contractions at a constant force of 25% MVIC, while the previous study had participants complete an isometric force matching tasks at constantly moving target force between 5-25% MVIC.[46] The increased task demand of a moving force task may have induced an alternative response in ACLR participants between the two studies.

The results of this study are in contrast to studies that have observed greater variability in quadriceps force during maximal isometric and isokinetic knee extension contractions in ACLR knees compared to healthy controls.[42,44,45] The combination of adaptations in neuromuscular function and alternative demands of maximal muscle contraction versus submaximal muscle contractions may have played a role in the contrasting findings. Altered sensory feedback from muscle and joint sensory receptors has been suggested as a mechanism for neuromuscular adaptations following ACLR.[47,56] This change in sensory input may place an abnormal constraint on the sensorimotor system leading to adaptations in neuromuscular motor unit recruitment and firing strategies, which have been identified as mechanisms that alters force control output.[57] At the neuromuscular level, researchers theorize that ACLR may lead to an inhibition of voluntary recruitment of type-II fiber motor units[58 59] which may lead to a reorganization of normal neuromuscular activation strategies.[34,47] The constraints of altered sensory feedback and motor

unit recruitment after ACLR may lead to alternative motor output during lower and higher demand tasks, such as maximal and submaximal contractions.[60] During maximal contractions, a high demand task for muscles, limitations on available neuromuscular strategies may manifest as greater variability in force output when the muscle is pushed to its maximal limit. Whereas during submaximal contractions, a less demanding task for the muscle, the limitations in available neuromuscular strategies may manifest as less complex force output, and therefore less variable. Variability in motor systems cannot be interpreted on a linear scale,[60] and therefore interpretation of higher or lower variability as better or worse muscle function should be done with caution. The lower variability in submaximal force control in the ACLR participants may appear to some as a gain in muscle function; however, this neuromuscular adaptation may present consequences to other aspects of muscle function. We do not know the implication of these adaptations have on knee function outside of this controlled laboratory task.

While ACLR participants demonstrated lower SD and error than controls during some of the force matching tasks, we can only speculate as to what this adaptation means for patient's overall function and muscle function. The ACLR patients had significantly lower self-reported knee function compared to healthy controls; however on average rated there knee function relative well (87-91%) considering they had a major knee joint surgery. We did not observe any correlation between measures submaximal force control and subjective knee function, despite previous studies showing a relationship between measures of maximum force control and subjective knee function.[42] We did observe a correlation suggesting that lower physical activity levels (Godin) were associated with lower SD and error during force matching tasks. These findings may suggest that the adaptations in quadriceps muscle function that present as lower SD and error during submaximal force matching tasks may be a limiting factor towards patients' ability to be physical active or a product of lower physical activity participation. We did observe a correlation suggesting that lower SD and error during submaximal contractions was related to weaker quadriceps. Quadriceps weakness is considered a post-traumatic impairment in muscle

function, which based on these results, may have similar neuromuscular origins to the changes we observed in submaximal force control.

We did not observe strong evidence to support time post-surgery being a major factor affecting submaximal force control in patients with a history of ACLR. Concentric force SD and RMSE, were lower in the Early, Mid and Late ACLR groups compared to controls, but there were no differences between ACL groups. Additionally, correlations between force control variables and time post-surgery were weak and non-significant. We hypothesized that ACLR knees later post-surgery, the group of ACLR participants that would theoretically be closest towards developing knee PTOA, would demonstrate altered submaximal force control compared to healthy controls based on evidence reporting altered submaximal force control in patient with knee OA compared to healthy controls. Knee OA is a condition marked by knee pain, which may explain the altered force control in this population. Experimental knee pain has shown to increase force SD and error during isometric, concentric, and eccentric force matching tasks.[53]

A limitation of the current study is that we can only speculate as to the neuromuscular mechanisms underlying the differences between ACLR and control knees and clinical indications of our findings. Poor subjective knee function is a clinical problem after ACLR, however our participants self-reported relatively high knee function on the KOOS (mean = 91%) which may limit our findings to patients doing relatively well after ACLR. Another limitation of our study was that force control was evaluated during a seated, non-functional testing task. This allows us to isolate function of the quadriceps muscles group; however, the task has limited generalizability towards the weight bearing dynamic demand that the muscles experience during daily functional activities.

CONCLUSIONS

During submaximal concentric and eccentric force matching tasks, participants with a history of ACLR produced quadriceps contractions with lower force SD and error than healthy

controls. Time post-surgery was not a major factor that effected submaximal force control. In ACLR participants, lower force SD and error during submaximal contractions was associated with weaker quadriceps strength and lower physical activity levels.

Table II-1. Demographic Variables in ACLR and Control groups.

	ACLR (n = 57)	**Control (n = 20)**	***P* value**
Sex $_{F,M}$	40 female, 17 male	13 female, 7 male	0.67
Age $_{years}$	22.9 ± 4.5	22.4 ± 3.2	0.62
Mass $_{kg}$	68.8 ± 15.2	68.9 ± 13.1	0.99
Height $_{m}$	1.71 ± .12	1.71 ± .13	0.71
KOOS $_{0\text{-}100}$	90.5 ± 6.6	99.3 ± 1.8	<.001[a]
IKDC $_{0\text{-}100}$	87.0 ± 8.8	99.5 ± 2.0	<.001[a]
Godin	68.4 ± 21.6	70.5 ± 17.9	.70
Time Post-Surgery, $_{months}$	51.8 ± 40.8	NA	NA
Graft-Type	Patella tendon: n = 28 Hamstrings: n = 21 Allograft: n = 8	NA	NA

[a] Significantly different between groups ($P<0.05$)

F = female, M = male, KOOS = Knee Injury and Osteoarthritis Outcome Score, IKDC = International Knee Documentation Committee Subjective Knee Evaluation, Godin = Godin Leisure-Time Activity Scale

Table II-2. Force Matching Variables during Isometric, Concentric, and Eccentric Force-Matching Tasks in ACLR and Control Groups

	ACLR group (n = 57)	Control group (n = 20)	*P* value	Effect-Size & 95%CI
Normalized MVIC, $_{Nm/kg}$	1.4 ± .4	1.7 ± .5	0.03 [a]	-0.57 (-1.09, -.05)
Isometric Contraction				
Standard Deviation, $_{Nm}$	.62 ± .23	.73 ± .31	0.10	-0.44 (-.95, .08)
Coefficient of Variation, $_{\%}$	2.8 ± 1.1	2.6 ± .7	0.37	0.19 (-.32, .70)
Root Mean Squared Error, $_{Nm}$	.79 ± .29	.93 ± .45	0.22	-0.38 (-.90, .13)
Concentric Contraction				
Standard Deviation, $_{Nm}$	2.3 ± .9	2.9 ± 1.0	0.01 [a]	-0.78 (-1.31, -.26) [b]
Coefficient of Variation, $_{\%}$	10.6 ± 5.0	11.9 ± 5.0	0.37	-0.25 (-.76, .26)
Root Mean Squared Error, $_{Nm}$	3.0 ± 1.0	3.8 ± 1.0	0.01 [a]	-0.73 (-1.25, -.21) [b]
Eccentric Contraction				
Standard Deviation, $_{Nm}$	2.1 ± .7	2.7 ± 1.1	0.02 [a]	-0.79 (-1.32, -.27) [b]
Coefficient of Variation, $_{\%}$	8.5 ± 4.0	9.3 ± 4.3	0.49	-0.18 (-.69, .33)
Root Mean Squared Error, $_{Nm}$	3.3 ± 1.3	3.7 ± 1.1	0.19	-0.34 (-.85, .17)

[a] Significantly difference between ACLR and control group (P<.05)
[b] Effect size 95% confidence interval does not cross zero
MVIC = maximum voluntary isometric contraction, 95% CI = 95% confidence interval

Table II-3. Force Matching variables during Isometric, Concentric, and Eccentric Force-Matching Tasks in Early, Mid, Late and Control Groups

	Early ACLR (n = 19)	**Mid ACLR (n = 20**	**Late ACLR (n = 18)**	**Control (n = 20)**
Normalized MVIC, $_{Nm/kg}$	1.4 ± .4	1.4 ± .4	1.5 ± .4	1.7 ± .5
Isometric Contraction				
Standard Deviation, $_{Nm}$	.64 ± .25	.61 ± .20	.63 ± .20	.74 ± .30
Coefficient of Variation, $_{\%}$	3.0 ± 1.2	2.7 ± 1.1	2.5 ± 1.0	2.6 ± .7
Root Mean Squared Error, $_{Nm}$	.78 ± .28	.72 ± .22	.88 ± .36	.93 ± .45
Concentric Contraction				
Standard Deviation, $_{Nm}$	2.2 ± .8 [a]	2.4 ± 1.0 [a]	2.1 ± .7 [a]	2.9 ± 1.0
Coefficient of Variation, $_{\%}$	11.3 ± 5.5	11.1 ± 4.9	9.3 ± 4.6	11.9 ± 5.0
Root Mean Squared Error, $_{Nm}$	2.9 ± .9 [a]	3.1 ± 1.1 [a]	3.1 ± 1.0 [a]	3.8 ± 1.0
Eccentric Contraction				
Standard Deviation, $_{Nm}$	2.0 ± .7	2.1 ± .7	2.1 ± .8	2.7 ± 1.1
Coefficient of Variation, $_{\%}$	8.3 ± 3.2	9.0 ± 4.3	8.2 ± 4.7	9.3 ± 4.3
Root Mean Squared Error, $_{Nm}$	3.0 ± .8	3.3 ± 1.5	3.6 ± 1.4	3.7 ± 1.1

[a] Significantly lower than control group (P<.05)
MVIC = maximum voluntary isometric contraction

Table II-4. Correlation Coefficients between Force Control Variables, Time Post-surgery, Normalized MVIC, KOOS, IKDC, and Godin scores in ACLR Participants

	Time Post-Surgery	Normalized MVIC	KOOS	IKDC	Godin
Concentric SD	-0.09	0.34 [a]	0.07	0.05	0.28 [a]
Concentric RMSE	-0.03	0.48 [a]	0.16	0.11	0.36 [a]
Eccentric SD	-0.01	0.16	0.18	0.12	0.11

a Significant correlation (*P<0.05)*
MVIC = maximum voluntary isometric contraction, KOOS = Knee Injury and Osteoarthritis Outcome Score. IKDC = International Knee Documentation Committee Subjective Knee Evaluation, Godin = Godin Leisure-Time Activity Scale

SECTION II: MANUSCRIPT III

EFFECTS OF PROLONGED PATELLAR TENDON VIBRATION ON QUADRICEPS STRENGTH IN ACL RECONSTRUCTED KNEES

ABSTRACT

Background: Quadriceps muscle dysfunction is common and persistent consequence following anterior cruciate ligament reconstruction (ACLR). Chronic quadriceps weakness has been associated with poor knee function and abnormal movement patterns. Post-traumatic adaptations in muscle spindle activity may be an underlying neural mechanism leading to quadriceps weakness. Patellar tendon vibration has been used to evaluate post-traumatic adaptations in quadriceps function that may be related to muscle spindle function; however this has not been studied in chronic ACLR knees. **Methods:** Fifty-one individuals with a history of ACLR and nine-teen healthy controls underwent baseline measures of quadriceps knee extension maximum voluntary isometric contraction (MVIC) at baseline and following a 20-minute patellar tendon vibration intervention. The raw-change and percent-change in MVIC from baseline to post-vibration were calculated. Interactions between groups and time were analyzed using repeated measures ANOVA and effect sizes. Correlations between raw-change, percent-change, time post-surgery, and baseline MVIC were performed using Pearson r correlation coefficients. **Results:** Both ACLR (P<.001) and control groups (P<.001) experienced significant increases in quadriceps MVIC following vibration. At baseline, there was no significant difference in MVIC between groups (P=.08), however post-vibration the control group demonstrated significantly greater MVIC (P=.01) and these findings were supported by effect-sizes. Effect size analyses suggest the ACLR group may have experienced a lower raw-change in MVIC compared to the control group, however there was no significant difference between groups (*P*=.06). Time post-surgery was positively correlated with raw-change (*r*=.29, *P*=.04) and percent-change(*r*=.28, *P*=.05). Baseline MVIC was negatively correlated with percent-change (r=.38, P=.01). **Conclusions:** Vibration increased quadriceps MVIC in ACLR and control knees. ACLR knees may have experienced an attenuated response to vibration compared to the control group. ACLR patients earlier post-

surgery may experience less change in MVIC after vibration. ACLR patients with weaker quadriceps may experiences a greater change in MVIC after vibration.

INTRODUCTION

Anterior cruciate ligament reconstruction (ACLR) and rehabilitation are the primary treatment option for physically active individuals that suffer an anterior cruciate ligament (ACL) injury and wish to return to physical activity. Quadriceps muscle weakness is an immediate and persistent consequence of ACL injury and ACLR[32] that can limit rehabilitation progress, is associated with to poorer knee function,[42,43] and may contribute towards the development and progression of post-traumatic knee osteoarthritis, a long-term consequence of ACLR.[4] The quadriceps muscles play and important role in knee joint protection as dynamic stabilizers and force attenuators during activities of daily living and sport. ACLR patients are at a high risk for the development knee joint osteoarthritis,[4] and quadriceps weakness may play a role in the progression of knee joint degeneration.[61,62] ACLR patients with evidence of early tibiofemoral joint space narrowing have demonstrated weaker quadriceps that ACLR patients with normal joint space narrowing and healthy controls.[61] Additionally, quadriceps weakness has been associated with altered knee biomechanics during gait, [12] another factor that may contribute towards the development of knee osteoarthritis over time.[8]

Arthrogenic muscle inhibition (AMI) is a reflexive neural impairment in muscle activation and an underlying mechanism of quadriceps weakness after ACLR.[34,47] Post-traumatic adaptations in proprioceptive input from peripheral receptors in the joint and muscle may disrupt the sensorimotor integration of excitatory and inhibitory neural pathways that contribute to activation of the quadriceps muscles.[47] One pathway for altered sensorimotor function after ACLR that has been studied is the gamma-loop, a spinal reflex circuit between gamma motorneurons, muscle spindles, and Ia afferent fibers, which acts to maintain excitatory sensory input from muscle spindles that synapses with reflexive alpha motor neurons and the central nervous system.[63] Muscle spindle feedback is essential for quadriceps activation and providing proprioceptive feedback for kinesthesia and regulating muscle stiffness.[64] Altered afferent

excitatory feedback from muscle spindles may be an underlying source for persistent quadriceps inhibition and weakness in the chronic ACLR knee that remains evident long after the initial trauma of injury.[47,56,63,65]

Vibration therapy has been used as an intervention to study and treat quadriceps neuromuscular inhibition in ACL injured,[65] ACLR,[56,66] and knee osteoarthritis[67,68] patients. Quadriceps targeted vibration, the application of high frequency mechanical stimuli to target quadriceps muscle tissues, has been applied locally to the patellar-tendon[47,56,65] or quadriceps muscle belly[66,69] or indirectly to the whole-body by standing on a vibrating platform.[66,68,69] Researchers have used vibration as an intervention to identify differences in motor responses between knee pathology patients[56,65,67] and healthy knees, and as a treatment to improve quadriceps muscle function.[66,68,69] Muscle spindles are sensitive to small changes in muscle length, and the repeated stretch of muscle spindles through vibration can alter muscle spindle firing rates.[70] In healthy knees, brief bouts of vibration are thought to increase excitatory input to alpha motor neurons thus increasing quadriceps performance, while prolonged vibration can cause a decrease in excitatory input from muscle spindles leading to a decline in quadriceps muscle strength.[70,71]

ACLR knees have demonstrated an abnormal response to prolonged patellar-tendon vibration compared to healthy controls. Quadriceps strength has been reported to decrease following prolonged patellar-tendon vibration in healthy participants whereas ACLR participants' strength does not change.[56,72-74] It was theorized that ACLR participants experienced a different quadriceps response to vibration due to altered muscle spindle and gamma-loop dysfunction secondary to injury.[56,72-74] This neural adaptation in muscle function presents a potential method to evaluate and treat an underlying impairment causing quadriceps weakness. However, studies have only been conducted in patients at early time-frames after ACLR (6-months to 2-years),[56,72-74] limiting our understanding of how this potential neural adaptation may contribute towards

chronic and persistent muscle weakness. Additionally, none of the previously published studies have examined the relationship between quadriceps weakness and the quadriceps muscles response to prolonged tendon vibration or examined the effects of vibration on ACLR knees with a patellar tendon bone-tendon-bone (BTB) graft. Therefore, the primary aim of this study was to examine the effects of prolonged patellar tendon vibration on quadriceps strength in ACLR knees at various time-frames post-ACLR. Secondary aims were to assess the relationship between quadriceps weakness and response to vibration in ACLR knees, and whether ACLR knees with a BTB graft demonstrated an altered response to vibration than those with a non-BTB graft.

METHODS

This study was completed in a controlled laboratory setting. Independent variables included groups (early ACLR, mid ACLR, late ACLR, all ACLR and healthy controls), as well as time (baseline and post-vibration). Dependent variables included quadriceps maximal voluntary isometric contraction (MVIC) torque and raw-change and percent-change in MVIC from baseline to post-vibration. All participants completed a baseline measure of knee extension MVIC, then a 20-minute vibration intervention, followed by a post-vibration measure of knee extension MVIC. Data collection was performed on a single test limb, the ACLR limb or a randomly selected limb for healthy participants. This study was approved by our University's institutional review board for health sciences research and all participants provided written informed consent.

Participants: Seventy total individuals volunteered for participation in this study. Fifty-one individuals with a history of primary, unilateral ACLR who were greater than 9-months post-surgery and had returned back to exercise/sport with no physical activity restrictions by a healthcare provider participated in this study (Table III-1). ACLR participants were excluded if they had a history of multi-ligament knee surgery, surgical complications, or bilateral knee joint surgery. There were no restrictions on participation based on ACLR graft type or a history of

meniscectomy or repair at the time of ACLR; however, participants with active meniscal symptoms (joint line pain, clicking) were not included. For analyses, ACLR participants were stratified into Early ACLR, 6-month to 2 years (n=16), Mid ACLR, 2 to 5-years (n=19), and Late ACLR, 5 to 15 years (n=16), groups based on their time post-surgery. Nineteen recreationally active individuals with no history of lower extremity injury or surgery and no current symptoms of lower extremity pain or neuropathy participated as healthy controls. All participants were between the ages of 18-35 and were recruited from our local university community. All participants completed the knee injury and osteoarthritis outcome score (KOOS),[23] the international knee documentation committee subjective knee evaluation form (IKDC),[24] and Godin Leisure-Time Activity Scale (Godin)[25] for descriptive purposes.

Quadriceps MVIC: Participants were seated a Biodex system III dynamometer (Biodex Medical Systems, Inc. Shirley, NY) with knees and hips flexed to 90° and 80°, respectively. The dynamometer axis was aligned with knee joint center and the torque arm was secured to the test leg just superior to the malleoli. Participants sat upright with back flat against the seat and arms across the chest. Quadriceps MVIC was a measure of peak torque produced during three knee extension MVICs at baseline and post-vibration. Participants were instructed to gradually increase contraction intensity and to hold the contraction steady at maximal contraction. Prior to baseline testing, participants completed four progressive warm-up contractions at 25, 50, 75, and 100% for testing familiarization. Post-vibration testing was performed immediately following the conclusion of vibration and no warm-up contractions were completed to avoid missing the effects of vibration.

Vibration: Vibration was delivered using a commercially available Deep-Tissue Percussion Therapeutic Massager (Wahl Clipper Corporation, Sterling, IL) with a modified reflex hammer applicator (Figure III-1). The applicator was aligned with the mid-substance of the patellar-tendon, central to the inferior patella and tibial tuberosity. Vibration was applied at a

frequency of 50 Hz,[56,72-74] amplitude of approximately 4 mm, force of approximate 30 N,[56,72-74] and for a continuous time of 20-minutes.[56,72-74]

Data Processing: Quadriceps MVIC torque data were digitized at 125 Hz and smoothed using a moving median filter (10 samples) in AcqKnowledge 4.2 (Biopac Systems, Inc., Goleta, CA). Torque data was converted to Newton*meters (Nm) and normalized by body mass (Nm/kg), the average torque over a 1.0-second epoch during peak MVIC was processed for each trial, and the mean of the 3 trials at baseline and post-vibration were used to calculate baseline MVIC and post-vibration MVIC. Raw-change in MVIC was calculated using the formula: Raw-change = (post-vibration MVIC − baseline MVIC). Percent-change in MVIC was calculated using the formula: %-change = $\left(\frac{post-vibration\ MVIC-baseline\ MVIC}{baseline\ MVIC}\right) \times 100$.

Statistical Analysis: We performed repeated ANOVAs to compare quadriceps MVIC before and after vibration between Early, Mid, Late, and Control groups (2x4, group by time) and all ACLR and control combined (2x2, group by time). One-way ANOVAs and independent t-tests were used to compare group demographics, raw-change, and %-change in quadriceps MVIC between Early ACLR, Mid ACLR, Late ACLR, and Control groups and between all ACLR participants and controls, respectively. Statistical significance was set at $P \leq .05$ for all tests, and omnibus tests were further analyzed with *post-hoc* independent t-tests, paired t-tests, and Cohen's d effect sizes and 95% confidence intervals (CI). Effect size point estimates were interpreted as <0.2 = minimal, ≥ 0.2 = small, ≥ 0.5 moderate, ≥ 0.8 = large.[29] Effect-sizes with 95% confidence intervals not-including zero were interpreted as indicating a meaningful effect. In ACLR participants, additional exploratory analyses to better understand the relationship between raw-change and %-change in MVIC after vibration and time post-surgery and quadriceps weakness were performed using Pearson r correlation coefficients and stepwise linear regression. Independent samples t-test were also performed to compare baseline MVIC, post-vibration

MVIC, raw-change, and %-change between ACLR participants with a bone-tendon-bone (BTB) graft and those with a non-BTB graft (hamstring or allograft).

RESULTS

Early, Mid, Late & Control: The Late ACLR group was significantly older than the Early ACLR ($P<.001$), Mid ACLR ($P<.001$), and Control ($P<.001$) groups ($F=12.7$, $P<.001$). KOOS was significantly lower in the Early ACLR ($P<.001$), Mid ACLR (P<.001), and Late ACLR ($P<.001$) groups compared to the control group ($F=12.4$, $P<.001$). IKDC was significantly lower in the Early ACLR ($P<.001$), Mid ACLR ($P<.001$), and Late ACLR ($P<.001$) groups compared to the control group ($F=13.5$, $P<.001$). There were no differences between groups for sex ($X^2= 2.7$, $P= .44$), mass ($F=.2$, $P=.87$), height ($F=.2$, $P=.88$), or Godin score ($F=1.8$, $P=.15$) (Table III-1).

There was no significant interaction ($F=1.5$, $P=0.23$) between time (baseline to post-vibration) and groups (Early, Mid, Late, Control) and no significant group main-effect ($F=1.8$, $P=.16$). ($F=99.8$, $P<.001$). Quadriceps MVIC significantly increased from baseline to post-vibration in the Early ACLR ($P<.001$, d=0.32 [-.38, 1.02]), Mid ACLR ($P<.001$, d=0.61 [-.04, 1.26]), Late ACLR ($P<.001$, d=0.70 [-.01, 1.41]), and Control ($P<.001$, d=0.63 [-.02, 1.28]) groups ($F=99.8$, $P<.001$). There was no difference in raw-change ($F=1.5$, $P=.23$) and %-change ($F=0.9$, $P=.43$) in MVIC between Early, Mid, Late and Control groups (Table III-2).

All ACLR & Control: The interaction between time (baseline, post-vibration) and groups (ACLR, Control) did not reach statistical significance ($F=3.6$, $P=0.06$) however, there was a significant time main-effect ($F=98.5$, $P<.001$) and group main-effect ($F=5.1$, $P=0.03$) (Table III-2). Due to the concern for type II error, we performed exploratory *post hoc* comparisons. Quadriceps MVIC significantly increased from baseline to post-vibration in the ACLR ($t=-8.7$, $P<.001$, d=0.51 [.11, .90]) and control group ($t=-4.6$, $P<.001$, d=0.63 [-.02, 1.28]).

Baseline MVIC (t=1.8, P=.08, d=-0.49 [-1.02, .05]) was not significantly difference between groups (Figure III-2). Post-vibration MVIC (t=2.6, P=.01, d=-0.70 [-1.24, -.16]) was significantly lower in ACLR than Control (Figure III-2). Raw-change in MVIC was not significantly different between groups (t=1.9, P=.06, d=-0.55 [-1.09, -.02]), but the effect size was moderate, towards lower raw-change in the ACLR group and 95% CI did not cross zero (Figure III-2). Percent-change was not significantly different between groups (t=1.0, P=.34, d=-0.26 [-.79, .27]), and the effect size was small, towards lower percent change in the ACLR group but 95% CI did not cross zero (Figure III-2).

Correlations & Regression in ACLR: In ACLR participants, there were a significant positive correlation between time post-surgery and raw-change (r=0.29, P=.04) and %-change in MVIC and (r=0.28, P=.05). There was a significant negative correlation between baseline MVIC and %-change (r= -0.38, P=.01) but not raw-change (r=-.15, P=.31) in MVIC.

Graft-Type: There were no significant differences in baseline MVIC (t=.3, P=.78), post-vibration MVIC (t=.2, P=.87), raw-change (t=-.3, P=.77), or %-change (t=-1.1, P=.28) between ACLR participants with a BTB autograft (n=26) and those with a non-BTB (n=25) graft (Table III-3).

DISCUSSION

Based on previous evidence,[56,72-74] we hypothesized that prolonged patellar tendon vibration would cause a significant decline in quadriceps MVIC in healthy controls and have no significant effect on quadriceps MVIC in ACLR knees. Contrary to the hypothesis, we observed significant increases in quadriceps MVIC in all ACLR knees, and healthy control knees; however, the magnitude of change in increase in quadriceps MVIC may have been attenuated in ACLR knees compared to control knees.

The patellar tendon vibration intervention that was used in the current study resulted in a different response than previous studies comparing the effects of prolonged vibration in ACLR and control knees.[56,72-74] The difference between our vibration intervention and previous studies was the vibration amplitude. Previous studies have reported a vibration amplitudes of 1.0-1.5 mm,[56,72-74] while the vibration device used in the current study delivered tendon stimulation at a larger amplitude of approximately 4.0 mm. The larger amplitude vibration may have elicited an alternative excitatory response on quadriceps muscle neurophysiology than what has been previously reported in studies of prolonged patellar tendon vibration with smaller amplitude vibration.[47,63,64,71] There is limited evidence to support this theory as the majority of studies using localized vibration applied directly to the tendon or muscle for either therapeutic or assessment purposes have all used small vibration amplitudes between 0.4-2.0mm.[56,66,72-75]

Our results may support the altered response to vibration in ACLR knees compared to control knees that has been previous reported in studies of prolonged patellar tendon vibration in ACLR knees and controls.[56,72-74] Both ACLR and control groups demonstrated a significant increase in MVIC from baseline to post-vibration; however, the magnitude of change may have been attenuated in ACLR knees. Effect size (d=.55) suggest that the raw-change in MVIC was an average of 0.17 Nm/kg lower in the ACLR group compared to the control group and since the 95% CI did not cross zero, the difference may be meaningful. Our results also suggest that baseline MVIC was not significantly different and had a small effect size between groups, while post-vibration ACLR MVIC was significantly lower than the control group and supported by a moderate effect size that did not cross zero, suggesting a meaningful difference. It is important to note that our findings agree with the current trend in the literature suggesting an abnormal response to vibration in ACLR knees compared to controls; however, our study observed an alternative response to vibration than what has been reported in previous studies. [56,72-74] Gamma-loop and muscle spindle dysfunction have been theorized to contribute to abnormal response to

vibration in ACLR knee, but there is limited neurophysiological evidence to support these theories. Additionally, there is no previous evidence to suggest an altered response to vibration is detrimental to muscle or knee function. In the current study, we observed a weak-moderate correlation between the %-change in MVIC and baseline MVIC suggesting that ACLR participants with weaker quadriceps experienced a greater percent increase in MVIC after vibration. It should be noted, there was no significant correlation between raw-change and baseline MVIC, so the correlation between baseline MVIC and %-change may be due to the fact that baseline MVIC is numerator of the calculation of %-change in MVIC.

We did not observe a significant interaction between the effect of vibration on quadriceps MVIC and our groups of ACLR patients at early, mid, and late time-frames and controls; however, our analyses of the association between time post-surgery and raw-change and percent-change in MVIC after vibration suggest that time post-surgery may be relevant. Our findings suggest that early after ACLR, participants may experience a smaller increase in quadriceps MVIC after vibration and longer time after ACLR was associated with larger magnitude response to vibration. If gamma-loop dysfunction and decreased muscle spindle excitation attenuates the quadriceps response to vibration, this finding may suggest that the greatest effects are occurring early after ACLR. This could suggest that over time the neural mechanisms causing decreased muscle spindle excitation resolve, or that over time the sensorimotor system develops an adaptation to upregulate these receptors to be more sensitive to mechanical stimuli.

On average, we observed an immediate increase in quadriceps strength of 21% in patients with a history of ACLR and 26% in healthy controls. A previous study testing the therapeutic effect of vibration on ACLR knees reported an average increase in normalized knee extension peak torque of 0.12 Nm/kg and effect-size of d=.40 following local muscle vibration,[66] while in the current study we observed an average increase of 0.28 Nm/kg and effect-size of d=.51 in our ACLR participants. The difference in magnitude of torque increase between the two studies may

be explained by differences in the application of the vibration stimulus. The previous study applied local vibration to the quadriceps muscle belly at 30 Hz, 1.6 mm amplitude, and for a series of 6 x 1-minute applications.[66] Future research is necessary to determine the most effective parameters for vibration therapy as a treatment for or assessment of quadriceps muscle dysfunction.

This was the first study of the effects of prolonged patellar tendon vibration in ACLR knees to include patients who had undergone a bone-tendon-bone autograft. Previous studies[56,72-74] have excluded those patients to avoid potential bias that the patellar tendon graft might have on the response to patellar tendon vibration. We observed no difference in quadriceps MVIC or raw and percent change in MVIC between ACLR participants with or without the bone-tendon-bone graft, suggesting future studies of patellar tendon vibration could utilize both patient populations, thus increasing the external validity of their findings to broader patient populations.

A potential limitation is that we did not have a placebo or non-vibration group. Within session reliability of knee extension MVICs has shown to very high (ICC=.99),[76] therefore we are confident the large increases in MVIC observed in this study were due to the vibration intervention. We also only measured the immediate effects of vibration on quadriceps MVIC. Vibration therapy in combination with therapeutic exercises may be clinically beneficial to improve quadriceps strength gains, therefore understanding the prolonged effects of vibration on muscle function in ACLR knees is necessary to translate these findings towards clinical practice.

CONCLUSIONS

Prolonged patellar tendon vibration caused a significant immediate increase in quadriceps strength in ACLR and control participants. ACLR knees may experience a smaller magnitude increase in quadriceps strength after vibration compared to healthy controls. In the ACLR participants, early time post-surgery was associated with a lower raw-change and %-change in MVIC after vibration. ACLR graft type did not affect the response to vibration in ACLR knees.

Table III-1. Demographic Variables in ACL Reconstruction Groups and Control Group.

	Early ACLR (n=16)	Mid ACLR (n=19)	Late ACLR (n=16)	All ACLR (n=51)	Control (n = 19)
Sex F,M	10 female 6 male	16 female 3 male	11 female 5 male	37 female 15 male	12 female 7 male
Age years	21.2 ± 4.1	20.6 ± 2.3	27.3 ± 4.3 [a]	22.8 ± 4.6	22.2 ± 3.3
Mass kg	66.6 ± 11.1	67.9 ± 9.8	69.6 ± 13.4	68.3 ± 11.3	69.5 ± 13.2
Height m	1.70 ± .09	1.72 ± .08	1.72 ± .11	1.72 ± .09	1.71 ± .14
KOOS 0-100	87.9 ± 7.1 [b]	91.2 ± 5.2 [b]	91.9 ± 7.7 [b]	90.2 ± 6.8 [b]	99.3 ± 1.9
IKDC 0-100	84.8 ± 9.2 [b]	86.1 ± 7.3 [b]	89.2 ± 10.4 [b]	86.6 ± 8.9 [b]	99.4 ± 2.1
Godin	66.4 ± 21.6	74.3 ± 13.3	58.8 ± 27.9	67.1 ± 21.7	70.8 ± 18.3
Time Post-Surgery, months	16.9 ± 5.9	40.1 ± 7.3	106.9 ± 32.6	53.2 ± 41.7	NA
Graft-Type	BTB = 6 Hamstring = 9 Allograft = 1	BTB = 11 Hamstring = 4 Allograft = 4	BTB = 9 Hamstring = 4 Allograft = 3	BTB = 26 Hamstring = 17 Allograft = 8	NA

[a] Significantly older than early, mid, and control groups (P<.001)
b Significantly lower than control group
KOOS = Knee Injury and Osteoarthritis Outcome Score, IKDC = International Knee Documentation Committee Subjective Knee Evaluation, Godin = Godin Leisure-Time Activity Scale, BTB = bone-tendon-bone graft

Table III-2. Baseline, Post-exercise, Raw-change, and Percent-change in MVIC in ACL Reconstructed and Control Groups

	Early ACLR (n=16)	Mid ACLR (n=19)	Late ACLR (n=16)	All ACLR (n=51)	Controls (n=19)
Baseline MVIC $_{Nm/kg}$	1.56 ± .73	1.48 ± .43	1.57 ± .49	1.53 ± .55	1.80 ± .64
Post-Vibration MVIC $_{Nm/kg}$	1.48 ± .43 [a]	1.74 ± .46 [a]	1.89 ± .41 [a]	1.81 ± .56 [a,b]	2.22 ± .66 [a]
Raw-change $_{Nm/kg}$	.24 ± .19	.27 ± .19	.32 ± .28	.28 ± .22	29.6 ± 27.9
Percent-change $_{\%}$	16.9 ± 16.0	19.8 ± 13.4	26.3 ± 27.1	20.9 ± 19.4	26.1 ± 21.4

[a] significantly greater post-vibration than baseline
[b] significantly lower in all ACLR than control
MVIC = Maximum voluntary isometric contraction

Table III-3. Baseline, Post-exercise, Raw-change, and Percent-change in MVIC in ACLR Participants with Bone-tendon-bone and Non-bone-tendon-bone Grafts

	BTB (n= 26)	**Non-BTB** (n= 25)
Baseline MVIC $_{Nm/kg}$	1.51 ± .54	1.55 ± .56
Post-Vibration MVIC $_{Nm/kg}$	1.80 ± .50	1.82 ± 63
Raw-change $_{Nm/kg}$	.29 ± .23	.27 ± .22
Percent-change $_{\%}$	23.8 ± 22.0	17.9 ± 16.2

MVIC = Maximum voluntary isometric contraction, BTB = bone-tendon-bone patellar tendon graft

Figure III-1. Vibration Device and Application Set-up

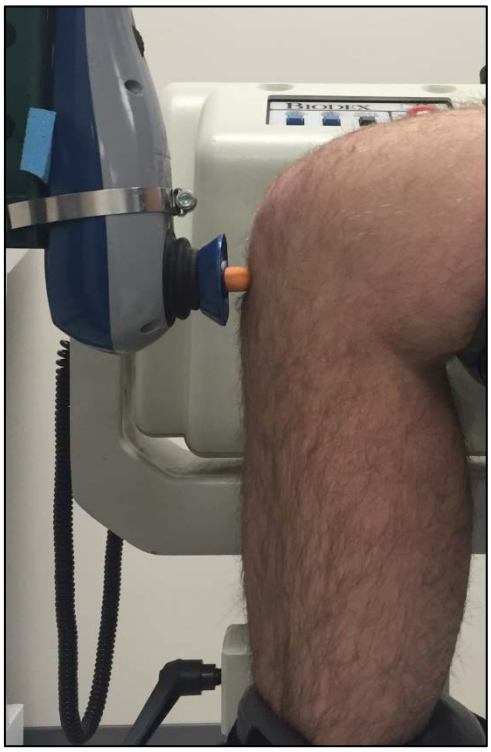
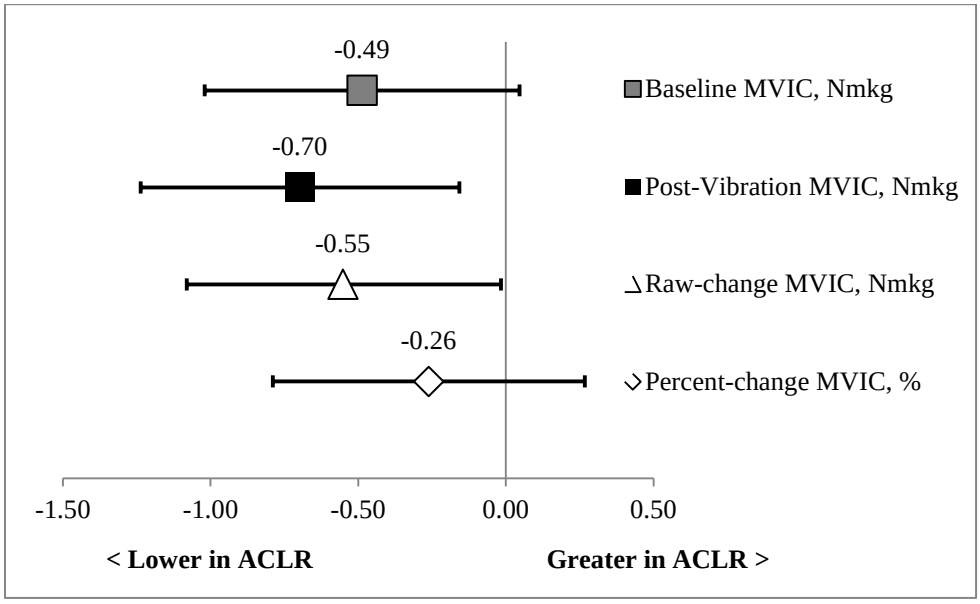


Figure III-2. Effect Size Point Estimates and 95% Confidence Intervals between ACLR and Control Group



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SECTION III: APPENDICES

APPENDIX A
The Problem

PROBLEM STATEMENT:

Degenerative joint disease, or osteoarthritis (OA), of the knee joint is one of the major causes of pain and physical disability in older adults.[2] Joint trauma in younger populations is considered a major risk factor for developing knee post-traumatic OA (PTOA) later in life. ACL tears are common and debilitating knee injuries for physically activity individuals. Generally, surgical reconstruction (ACLR) is the treatment option utilized for ACL deficient (ACL-D) patients wishing to return to sport and exercise. Evidence has shown that patients with a history of ACLR have an increased risk for early-onset OA[3-5] compared to individuals without a history of knee injury. This typically geriatric condition associated with the "wear and tear" of articular surfaces over a lifetime is now presenting in younger adults within a history of ACLR. Patients are experiencing chronic knee-related disability and reduced activity levels,[6] predisposing them to the chronic health conditions associated with physical inactivity.[7] No successful treatment has been identified for patients with knee OA; therefore the best option for patients and clinicians is early identification of modifiable risk factors and intervention. Diminished quadriceps strength[8] and abnormal lower extremity gait biomechanics[9] are modifiable risk factors for the progression of OA.

Abnormal ambulatory mechanics have been implicated as factor contributing to the progression of PTOA under the hypothesis that the natural repetitive and cyclic

loading of joint surfaces that occurs during daily walking may be compromised in the presence of abnormal lower-extremity locomotion patterns.[9] Quadriceps avoidance gait,[10] a reduced peak external knee flexion moment during the stance phase of gait, has been observed in patients with a history of ACLR,[11] and is considered a consequence of diminished quadriceps muscle activity. Quadriceps muscle dysfunction, traditionally quantified as "weakness" or a reduced maximal knee extension torque, is a common and persistent impairment in patients after ACL injury and reconstruction.[12] Patients with a lower quadriceps muscle strength symmetry index have demonstrated lower peak internal knee extension moment compared to health controls during level walking.[13] Persistent deviations in normal gait, such as the quadriceps avoidance gait pattern, may contribute to the progression of knee OA after ACLR; however, the chronic effects of ACLR on gait are not well understood.

Measures of quadriceps strength, traditionally quantified as the maximal force or torque production during isometric or isokinetic contractions, are the most commonly reported and clinically utilized to evaluate quadriceps muscle function pathological patients. While these measures provide valuable information regarding the maximal contraction capacity of the muscle to produce force, they are limited in the fact that maximal contractions are not routine in daily physical activities or sport. Measures of submaximal isometric and isokinetic quadriceps force control have been used to evaluate the ability of knee pathology patients to produce steady and accurate muscle contractions.[14,15] Quadriceps force control, specifically at submaximal intensities, may be a valuable determinant of muscular performance that more closely relates to quadriceps contractions that are utilized during daily functional tasks such as walking. Patients with

knee osteoarthritis have demonstrated poor accuracy and steadiness during submaximal concentric and eccentric force matching tasks.[14,15] In ACLR knees, patients have demonstrated greater fluctuations in force during maximal isometric knee extension contractions compared to healthy control knees,[16,17] however the clinical relevance of those findings can be questioned due to use of maximal contraction. There is minimal evidence regarding the use of submaximal force control measures in ACLR populations, however may be valuable in identify factors that contribute to abnormal joint loading and lower extremity control during daily and physical activities.

Diminished quadriceps muscle function may be the product of underlying changes in neural pathways secondary to ACLR injury.[18] Changes in the discharge of sensory receptors in the damaged knee may alter excitability of multiple spinal and supraspinal pathways that contribute to activation of the quadriceps muscles.[18] One pathway that has been studied in the quadriceps is the gamma-loop, a spinal reflex circuit between gamma motorneurons, muscle spindles, and Ia afferent fibers, which acts to maintain accurate sensory information to the CNS and reflexive motorneuron excitability to muscle.[19] Normally, the gamma-loop plays an important role in alpha-gamma co-activation and regulating muscle stiffness.[20] Researchers have observed an abnormal response to prolonged patellar tendon vibration in ACL-D,[21] ACLR[22,23] and OA[24] knees when compared to healthy controls. Healthy knees experienced a normal vibration-induced decline in peak knee extensor torque, while pathological knees did not.[21-24] Prolonged vibration is thought to reduce Ia afferent signals, and therefore quadriceps motor output, due to repetitive stretching of homonymous muscle spindles.[25] Researchers theorized that the abnormal response to vibration in pathological knees may be due to changes in

gamma-loop activity, and have coined the abnormal response to vibration "gamma-loop dysfunction".[21,22,24] This response to vibration has only been examined in patients during the early stages after ACLR, however this technique could provide insight into underlying neural mechanisms associated with quadriceps muscle dysfunction that would be valuable when developing future intervention programs. There is no current evidence regarding the relationship between quadriceps gamma-loop dysfunction and quadriceps muscle performance. In ACLR patients, quadriceps gamma-loop dysfunction has only been measured in patients early after surgery; the chronicity of this muscular abnormality is unknown.

SPECIFIC AIMS:

This is a descriptive laboratory study with and overarching aim to better understand biomechanical, muscular, and neural adaptations that occur in patients with ACLR knees. We are particularly interested in what role time since surgery plays in these adaptations due to the lack of evidence and potential implications towards long-term outcomes. Therefore, the primary analysis of each project will be utilize a cross- sectional analyses of groups of patients at early (9 month to 2 years), Mid (2 years to 5 years), and Late (5 years +) stages of ACLR chronicity and a group of healthy controls.

The aims of project #1 are to investigate inter-differences in knee and hip kinetics and kinematics during walking and jogging in groups of patients at sequential stages after ACLR surgery.

The aims of project #2 are to investigate differences in submaximal quadriceps force control and strength in ACL reconstructed and healthy control knees. We will examine differences between ACLR groups at different time-frames post-surgery and

examine correlations between measures of quadriceps force control, time post-surgery, quadriceps strength, physical activity levels, and subjective knee function.

The aims of project #3 are to investigate differences in quadriceps gamma-loop dysfunction, using the prolonged tendon vibration technique, in ACLR patients and controls. We will also examine differences in groups of patients in sequential time-frames after ACLR surgery. We will also investigate the relationship between the change in strength following vibration and time post-surgery and baseline quadriceps strength.

PROJECTS AND DESIGNS:

I. Project:

Walking and Jogging Biomechanics in Patients at Early, Mid, and Late Time-frames after ACL Reconstruction Surgery

I. Research Question:

1. Do ACL reconstructed patients at different time-frames post-surgery, early, mid, and late, demonstrate inter-limb adaptations in knee and hip biomechanics during walking and jogging?

I. Experimental Design:

Independent Variables

- Limb: Involved limb (ACLR or random), Uninvolved limb
- Groups: 1) Early ACLR: <2 years post-surgery
  2) Mid ACLR: 2-5 years post-surgery
  3) Late ACLR: >5 years post-surgery
  4) Healthy control group

Dependent Variables

- Walking and jogging hip and knee kinetics and kinematics
    - Sagittal and frontal plane

Analyses

- Time series graphs of means and 90% confidence intervals(CI) of involved and uninvolved limbs with each ACLR group and control group.
    - Significant difference = regions that 90% do not overlap for 3 consecutive percentages of 100% gait cycle.
- Average differences and effect-sizes calculated for regions of significant differences.

I. Experimental Hypotheses:

- The Early ACLR group will demonstrate the greatest inter-limb differences in the sagittal plane.

***II. Project*:**

Submaximal Quadriceps Force Control in ACL Reconstructed Knees

II. Research Question:

1. Is quadriceps force control and strength different between early, mid, and late ACL reconstructed knees and healthy controls?
2. Is quadriceps force control and strength difference between all ACL reconstructed knees and healthy controls?
3. In ACLR patients, is quadriceps force control associated with strength and subjective knee function?

II. Experimental Design:

Independent Variables

- Group: Early ACLR, Mid ACLR, Late ACLR, Healthy control
- Group: ACLR & Control

Dependent Variables

- Submaximal isometric force control

  - *Coefficient of variation (CV), Root Mean Square Error*

- Submaximal isokinetic force control

  - *Coefficient of variation (CV), Root Mean Square Error*

Analyses

- One-way ANOVAs
- Independent samples t-tests
- Pearson correlation coefficients

II. Experimental Hypotheses:

1. Quadriceps force control and strength will be different between groups.

   a. Healthy group = strongest, force control.

   b. Early ACLR group = weakest, lowest force control in ACLR groups

   c. Mid ACLR group = strongest, greatest force control in ACLR groups

   d. Late ACLR group < Mid ACLR group.

2. Quadriceps force control and strength will be different between ACLR and controls groups.
3. Poor quadriceps force control will be associated with weaker strength and poorer subjective knee function.

III. Project:

Effects of Prolonged Patellar Tendon Vibration on Quadriceps Strength in ACL Reconstructed Knees

III. Research Question:

1. Is the vibration-induced change in knee extension torque different between early, Mid, and Late ACL reconstructed knees and healthy controls?
2. Is the vibration-induced change in knee extension torque different between all ACL reconstructed knees and healthy controls?
3. Is the vibration-induced change in knee extension torque associated with quadriceps strength?

III. Experimental Design:

<u>Independent Variables</u>

- Group: Early ACLR, Mid ACLR, Late ACLR, Healthy control
- Group: ACLR & Control
- Time: Baseline, Post-vibration

<u>Dependent Variables</u>

- Mass normalized peak isometric knee extension strength
- Raw-Change in peak knee extension torque
- Percent-Change in peak knee extension torque

<u>Analyses</u>

- One-way ANOVA
- Pearson's product-moment correlation coefficients

III. Experimental Hypotheses:

1. Vibration-change will be different between ACLR groups.

    a. Healthy group = greater negative vibration-change compared to ACLR groups.

    a. Early ACLR group = least negative vibration-change in ACLR groups

    b. Mid ACLR group = greatest negative vibration-change in ACLR groups

    c. Late ACLR group < negative vibration-change than the Mid group.

2. Vibration-change will be weakly associated with measures of quadriceps strength.

ASSUMPTIONS, DELIMITATION, & LIMITATIONS

Assumptions

- Participants provided accurate information regarding lower-extremity injury and surgery history.
- Participants provided maximal effort and attention during all knee extension assessments.
- Knee extension contractions were indicative of quadriceps muscle function.
- Prolonged patellar tendon vibration induced a change in normal muscle spindle activity.
- Participants gait patterns during experimental treadmill walking reflect normal daily walking gait.
- Reflective markers adhered to skin were indicative of bone and joint motion.

Delimitations

- ACLR participants were limited to primary, unilateral ACLR surgery with no additional ligamentous reconstruction or surgical complications.
- ACLR participants were a minimum of 6-months post-surgery.

- There were no restrictions on ACLR graft type or rehabilitation protocol.
- Repeated knee extension tasks may result in muscular fatigue.
- Primary gait comparisons were made between involved and uninvolved limbs within each group.

Limitations

- The Late ACLR group ended up being statistically significantly older than the other three groups.
- Gait testing was performed at standard speeds that did not match all participants normal walking or jogging speeds.
- We did not measure trunk biomechanics to support theoretical adaptations in frontal plane gait.
- We did not measure hip muscle function to support theoretical adaptations frontal plane in gait.
- Isokinetic force matching tasks were normalized to participant's maximal isometric contraction, not maximal isokinetic contraction.

OPERATIONAL DEFINITIONS & EQUATIONS

Early ACLR group: Participants with a history of primary, unilateral ACL reconstruction surgery less than 2-years prior to the date of their initial testing visit.

Gamma loop dysfunction: A term used to describe a dysfunction in the normal neural network between the gamma motorneurons, muscle spindles, and Ia afferent signals in the quadriceps in ACL deficient, ACL reconstructed and knee osteoarthritic knees. Gamma loop dysfunction has been identified in previous

studies using the percent change in knee extension torque following prolonged patellar tendon vibration.

Healthy control group: Participants will be age and sex matched to ACLR participants and will have no history of lower-extremity joint injury or significantly lower-extremity muscle injury.

Isokinetic force control: A measure of the ability of a participant to match and sustain a target knee extension torque (25% MVIC) during concentric and eccentric isokinetic contractions at 10 degrees/second. The knee moves through range of motion from 15-65 degrees of flexion. This measure is quantified using the coefficient of variation and the root mean square error relative to the target force.

Isokinetic strength: The average peak torque over a series of 8 isokinetic maximal knee extension contractions at 90 and 180-degreees per second.

Isometric force control: A measure of the ability of a participant to match and sustain a target isometric knee extension contraction at 25% and 50% of their maximal contraction. This measure is quantified using the coefficient of variation and the root mean square error relative to the target force.

Late ACLR group: Participants will have a history of primary, unilateral ACL reconstruction surgery greater than 5-years prior to the date of their initial testing visit.

Mid ACLR group: Participants with a history of primary, unilateral ACL reconstruction surgery between 2-years to 5-years prior to the date of their initial testing visit.

Mid-substance of patellar tendon: The vertical midsection between the most distal aspect of the patella and the most proximal aspect of the tibial tuberosity. This will be the standardized location for tendon vibration application.

Peak Knee Flexion Moment: Peak internal sagittal knee moment that resists the external forces that move the knee into flexion during the stance phase of gait.

Prolonged patella tendon vibration: A percussion vibrator applied to the mid substance of the infrapatellar tendon with the following parameters: 20 minutes, 50 Hz, ~30Nm.

Quadriceps avoidance gait: A reduced sagittal moment during gait secondary to joint injury.[10]

Quadriceps force control: The ability to produce a smooth, accurate knee extension contraction.

Stance phase of gait: Time during the gait cycle during which the limb is in contact with the ground. This phase begins at initial contact and ends just prior to toe off.

Vibration-Change: The percentchange or raw-change in peak knee extension torque following 20-minutes of prolonged patellar tendon vibration.

Equations:

Coefficient of variation (CV)*[16,17]*: $= \frac{\text{Force Standard Deviation}}{\text{Mean Force}} \times 100$

Root Mean Square Error (RMSE)*[26]*: $= \left|\text{Target force - Contraction force}\right|$

Percent-Change in vibration[22,23]*:* $\frac{\text{Post-vibration torque - Baseline torque}}{\text{Baseline torque}} \times 100$

Raw Change in vibration[22,23]***:*** Post-vibration torque - Baseline torque

INNOVATION:

The aims of this study are to examine changes in gait biomechanics, quadriceps motor control, and quadriceps gamma-loop dysfunction that occur in patients at sequential stages after ACLR. The clinical goals for a patients recovering from ACLR are 1) to restore knee joint function and allow patients to progressively and safely return to desired physical activity levels, and 2) to limit the potential cascade of joint deterioration and degeneration that these patients are not at risk for due to their knee injury. However, evidence has shown that ACLR is still a major risk factor for OA. Researchers have studied alterations in gait, deficits in muscle performance, and changes in neural pathways in an attempt to identify modifiable areas of post-traumatic musculoskeletal function. Investigating each of these factors is important due to the interdependence on one on the others.

Interventions target towards improving joint mechanics would involve a combination of achieving optimal muscle performance and retraining correct movement patterns. Identifying a relationship between laboratory measures of quadriceps motor control and quadriceps avoidance gait may provide scientists and clinicians a new dimension of muscle function to focus research and rehabilitation efforts. Current rehabilitation efforts primary focus on improving quadriceps muscle strength and while these measures provide valuable information regarding the maximal capacity of the muscle to produce force, they are limited in the fact that maximal quadriceps contractions are not utilized for daily physical activities. The most appropriate surrogate assessments of functional muscle performance may be measures of quadriceps motor control due to

the focus on submaximal contractions and the ability of patients to produced coordinated and controlled contractions.

Gamma-loop dysfunction is often discussed as a potential neural mechanism for quadriceps muscle dysfunction. Current experimental evidence regarding gamma-loop dysfunction is limited in the quantity of studies, the populations studied, and a lack of evidence exploring the relationship between the presence of gamma-loop dysfunction and quadriceps muscle dysfunctions. If gamma-loop dysfunction is associated with quadriceps muscle dysfunction, research efforts can then be directed towards developing intervention strategies targeted towards influencing the gamma-loop. Theoretically □ such avenues may include neuromuscular electrical stimulation with parameters targeting intrafusal fibers, or interventions targeting cutaneous receptors, such as cryotherapy or transcutaneous electrical nerve stimulation, since experimental evidence suggests the gamma-loop is influenced by cutaneous receptors.[27]

APPENDIX B
Literature Review

ACL Reconstruction

Injury to the anterior cruciate ligament (ACL) often involves a complete rupture of the ligament. Patients experience significant joint instability and lower extremity functional disability after ACL injury. Patients wishing to return to a physical activity lifestyle after ACL injury often elect for ACL reconstruction (ACLR) surgery. ACLR surgery involves reconstructing the static restraint once maintained by the ACL using autograft or allograft tissues. Meniscal injuries are the most commonly diagnosed concomitant condition at the time of ACL reconstruction, and arthroscopic excision of joint structures and excision of meniscus are the most common concomitant procedures at the time of surgery.[28]

Recent estimates suggest that about 130,000 ACLR surgeries, or 43.5 per 100,000 person years, were performed in the US in 2006. Based on the increase from 32.9 per 100,000 years (about 86,687) in the 2006, evidence suggests that the incidence of ACLR surgeries is increasing. The average age of an ACLR patients in 2006 was 29±13 years, with the greatest number of ACLR surgeries performed on patients less than 20 years old (42%), followed by patients 20-29 years old (21%).[28]

Despite relatively high return-to-sport rates for an injury that was once considered "career ending", outcomes after return-to-sport are not as promising for patients with a history of ACLR. Short-term, ACLR patients are at increased risk for a second ACL

injury.[29] Long-term, patients experience greater subjective knee disability, lower physical activity levels and physical health,[6] and are at a greater risk for developing degenerative joint disease than individuals without a history of ACL injury and surgery.

Short-term Outcomes

The immediate goal for the majority of patients after ACLR surgery is a return to previous levels of physical activity. A meta-analysis of return to sport rates in patients after ACLR (studies published after year 2000) found that about 85% of patients return to some level of sport after surgery, 64% return to pre-injury level of sport, and 56% of patients return to competitive sport.[30] The most commonly reported reasons for patients not returning to pre-injury level of sport included fear of re-injury (19%), problems with function of the ACLR knee (13%), and non-knee related reasons (18%).[30]

Recent study of The Swedish National Knee Ligament Register observed that 1.82% (308/16,930) of patients had an ACLR revision during a 2-year follow-up after ACLR.[31] The incidence was highest in participants 13-19 years old (3.47%), followed by participants 20-29 years old (1.80%), then >30 years old (0.74%).[31] Another study observed that 6.6% (4/63) of patients experienced an ipsilateral ACL injury and a 19% (12/63) experienced a contralateral ACL injury during a 12-month follow-up after initial ACLR.[29] The incidence of ipsilateral and contralateral ACL injury was 0.54 per 1000 and 1.38 per 1000 and athletic exposures, respectively.[29]

Long-term Outcomes

Lower Knee Function and Physical Activity

Long-term subjective knee-related disability is commonly reported in patients with a history of ACLR. Patient reported outcomes, such as the International Knee

Documentation Committee Subjective Knee Evaluation (IKDC), have been lower in patients with a history of ACLR compared to healthy controls.[32]

Participants with a history of ACLR have also reported decreased physical activity levels, as measured by the Tegner activity scale, compared to age and sex matched controls.[6]

Degenerative Joint Disease

Osteoarthritis is the most common form of arthritis and the condition accounts for physical disability word-wide. Osteoarthritis is disease that progresses with age and has no known treatment. Knee joint trauma, such as ACL injury and reconstructive surgery, have been suggested as important risk factors towards the progression of articular cartilage degenerative, or osteoarthritis (OA), of the knee.[5,33] A recent systematic review of OA estimated that 36% of ACLR knees will develop evidence of knee OA in the first decade post-surgery, with 48% developing knee OA by the second decade.[34] These findings are concerning considering the greatest number of ACLR procedures are performed on patients younger than 20 years.[28]

In a study of 210 ACLR patients, 71% of ACLR knees demonstrated radiographic evidence of tibiofemoral OA (Kellgren-Lawrence ≤ 2)[35] at 10-15 year follow-up, while only 25% of contralateral knees had evidence of OA.[35] Moderate to severe OA ($KL \geq 3$), was present in 24% of ACLR knees and 6% contralateral knees.[35] Concomitant injuries, specifically to meniscal and articular cartilage, increase the risk for knee OA associated with ACLR. In a study of 112 participants with combined ACLR and meniscal/cartilage injury and 69 participants with an isolated ACLR, the prevalence of radiographic OA

(KL≥2) was significantly greater in those with combined injuries (80%) compared to those with isolated injuries (62%).[36]

Adaptations in lower-extremity gait biomechanics and muscle function have implicated as contributing risk factors towards the progression of OA.[9] Additionally, deficits in knee extensor strength have been associated with in increased risk of developing OA in both men and women.[8]

Sensorimotor Adaptations

Researchers theorize that poor outcomes after ACLR may be related to adaptations in the sensorimotor system that occur secondary to joint trauma.[1] Altered lower-extremity motion biomechanics and joint loading, diminished strength, activation, and control of muscles, and deficits in conscious knee proprioception have been observed in patients after ACLR and may represent disruptions or disorganization within the neural pathways of the sensorimotor system.[12] These adaptations are thought to manifest secondary to the disruption of articular sensory receptors that occurs with ACL injury and surgery. Afferent signals from the mechanoreceptors in the knee joint have direct and indirect influences at spinal and

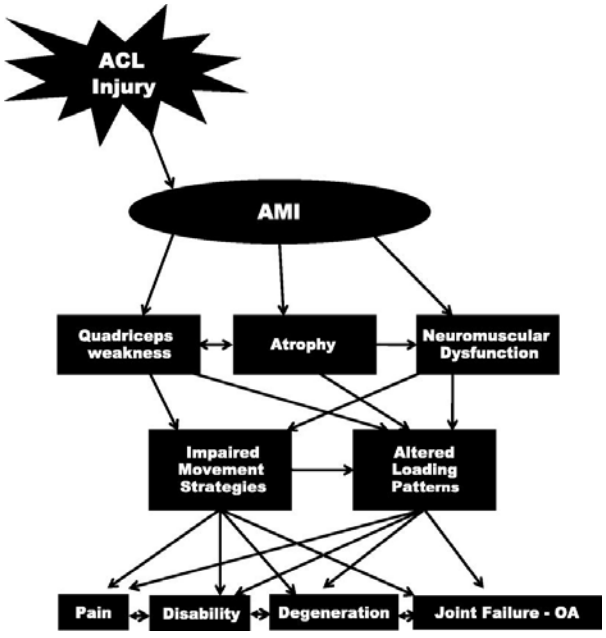


Figure B-1. Schematic diagram of the theoretical relationship between sensorimotor adaptations and knee OA and disability (Palmieri-Smith 2009)[1]

supraspinal levels of the sensorimotor system and influence the spinal and supraspinal pathways that control movement and muscle activity.

Supraspinal pathways control the motor programs or central pattern generators that regulate movement patterns such as locomotion and control descending signals to voluntary contract muscles. Changes in the activity of supraspinal pathways may contribute to abnormal lower-extremity movement strategies and impaired voluntary muscle activation after ACLR.

Spinal pathways can directly, via spinal reflexes, or indirectly, via ascending projections to supraspinal pathways, influence muscle activity and proprioception. Arthrogenic muscle inhibition (AMI) describes diminished muscle activity in response to articular trauma.[18] Persistent deficits in quadriceps strength, activation, and control are considered a product of AMI. Several spinal reflex pathways have been implicated as potentially contributing to AMI, including the gamma-loop, Ib inhibitory pathways, and flexion reflex pathways.[18]

Gait Adaptations

Abnormal lower-extremity gait patterns are common following ACLR[11] and have been implicated as a contributing factor to the pathogenesis of knee joint degeneration.[9] Specific attention has been given to changes in sagittal plane knee kinetics during gait in patients with a history of ACLR due to the overwhelming evidence suggesting quadriceps muscle function is impaired after ACLR. During gait, the quadriceps muscles eccentrically contract during the loading phase to control sagittal plane joint loading. Following ACLR, impaired quadriceps muscle function may expose joint surfaces to altered or excessive loads. The “quadriceps avoidance” gait strategy was first observed in

patients with ACL deficient knees[10], however evidence suggests that patients with ACLR knees also demonstrate this abnormal gait strategy[11]. Quadriceps avoidance gait is characterized by a reduced knee flexion moment during the stance phase of gait, and is theorized to represent an adaptation in gait that relies less on quadriceps activity during the stance phase.

A systematic review published in 2010 found four studies[13,37-39] meeting their criteria that evaluated differences sagittal plane knee moments during walking gait in ACLR and healthy control knees[11]. Effect sizes between ACLR and control knees ranged from -.40 to -1.77 with a weighted average effect size of -.94, suggesting the magnitude of the sagittal plane moment was less in the ACLR knees[11]. ACLR participants in the included studies ranged from about 3-months to 12-months post-surgery, suggesting a relatively acute time-frame post-surgery.

A limitation of previous evidence regarding walking gait in ACLR knees was that analyses were generally performed at a single time-point and in the acute stages after surgery. Investigating gait patterns over time after ACLR may promote a better of understanding of the presence and progression of abnormal gait patterns following ACLR. A recent study longitudinally assessed walking gait in the ACLR knee and contralateral healthy knee of 16 patients at an average of 10-months and 3-years after ACL surgery.[40] The study observed no significant effect of time on external knee flexion moment.[40] A significant limb-by-time effect was observed for the external knee extension moment, suggesting knee extension moment increased in the ACLR knee but not the contralateral[40]. This may attributable to the increased knee extension range angle at the terminal phase of stance in the ACLR knee[40]. Another recent study examined gait

patterns in 20 female ACLR patients at an average of 5-years (±3) post-surgery and 20 healthy controls.[41] ACLR knees demonstrated a reduced sagittal plane knee moment during walking compared to health control knees (d= -1.20 [-1.88, -.53]).[41] ACLR knees demonstrated greater initial impact force and greater average loading rate.

A relationship between quadriceps weakness and quadriceps avoidance gait has been observed. One study observed that participants with weak quadriceps (n=10), quantified as a limb symmetry index less than 80%, had a reduced sagittal knee moment compared to healthy controls (n=8).[13] There was no difference between participants with strong quadriceps (n=8), quantified as a limb symmetry index greater than 90%, and healthy controls.[13] A moderate correlation was observed between quadriceps strength symmetry and sagittal plane kinetics, suggesting that as quadriceps strength increased, so did the sagittal plane moments.[13] These findings support the theory that reduced sagittal moments are related to diminished quadriceps function.

The external knee adduction moment has become a popular gait variable of interest in patients with a history of ACLR.[40,42-45] The role of the knee adduction moment in the development and progression of idiopathic knee osteoarthritis (OA) has been extensively studied.[46] The knee adduction moment is thought to represent greater medial knee joint loading,[47] leading to the higher rates of medial compartment tibiofemoral OA.[48] Evidence studying the presence and role of an altered knee adduction moment in ACLR knees has been conflicting.[49] Reports of significantly higher[43] and lower[40,44,45,50] knee adduction moments have been reported in patients with a history of ACLR compared to contralateral knees[40,44,45] and healthy controls knees.[43,50] A recent systematic review observed a trend in studies suggesting that walking knee adduction moment was

lower in ACLR participants early post-surgery (~1-year) and higher in ACLR participants in later phases (5-years) post-surgery compared to healthy controls.[49]

Current methods of gait analysis include the use of three-dimensional motion capture systems that use electromagnetic sensors or high-speed cameras and anatomic markers to track lower-extremity segment motion and force plates to measure ground reaction forces. Kinematic variables are calculated using anatomic joint centers and segment motions, and kinetics variables are calculated using inverse dynamics.

Quadriceps Force Control and Knee Pathology

Knee extension contractions are commonly performed in clinical and research practices to assess quadriceps muscle function after ACLR.[51-53] Recently, researchers have identified impairments in quadriceps muscle function by examining the quality, or steadiness, of contractions during maximal and submaximal knee extension contractions. Knee extension force control, also referred to as “variability”, “steadiness”, or “accuracy”, has been used as a means to quantify deficits quadriceps neuromuscular control. Quadriceps muscle force control refers to the ability to produce a steady and accurate muscle contraction during static or dynamic contraction tasks.[54] Deficits in quadriceps strength, the muscle capacity to produce maximal torque, are more commonly reported in clinical and research settings. While strength represents one aspect of muscle function, maximal muscle contractions are atypical during daily physical activities. Impaired contractions steadiness or control may indicate abnormal motor output variability,[55] which could contribute to irregular lower extremity movement patterns and increased joint loads during physical activities.

Deficits in knee extension force control have been observed in a variety of knee pathologies, including ACLR, ACL-D, and OA knees, however methods and quantification of force control have varied between studies. A summary of current evidence examining knee extension contraction control in these patients groups is presented in Table B-1. The majority of studies in ACLR patients have used maximal knee extension contractions, either isometric[16,17] or isokinetic[56], to quantify force control. These studies observed impaired knee extension force control in ACLR knees compared to health control,[16,17,56] which was associated with single leg hopping performance[56] and subjective knee function.[16] The use of maximal knee extension contractions, a type of contraction not common during daily physical activities, could be considered a limitation of these studies. Only one study has examined force control during submaximal isometric knee extension contractions.[26] ACLR participants demonstrated impaired force accuracy while attempting to match a cyclical target alternating between 5-30% of MVIC.[26]

Impaired force control has also been observed in ACL-D knees, primarily during maximal isokinetic knee extension contractions[56,57]. Associations between knee extension force control and single leg hop performance have been observed in ACL-D knees.[56,57]

Impaired knee extension force control has also been observed in OA knees, primarily during submaximal isokinetic knee extension contractions. OA knees have demonstrated poor force control during eccentric[14] and concentric[14,15] knee extension contractions compared to age-matched control knees. One study examined the association

between submaximal isometric knee extension steadiness and frontal plane knee moments during walking gait, but found no relationship between the two measures.[58]

Table B-1: Quadriceps Force Control in Knee Pathology Literature Review

ACL Reconstructed				
Article	Participants	Testing	Force Control Measure	Pertinent Findings
Bryant et al. 2009[56] *J Bone Joint Surgery*	- 25 unilateral, ACLR (15.7±5.5 mo surgery) - 33 healthy controls	- Max isokinetic exten/flex (180 °/s) - Hamstring EMG (avg ST & BF) - Timed SL hopping task	- Mean instantaneous frequency (wavelet transform). 3 trials with highest torque. 20-70° flexion. ↑Instant freq = ↓control	- ↑Instant freq in ACLR vs control. *Combined w/ ACL-D - Mod corr between ↑Instant freq & ↑HS activation - ↑Instant freq related to faster hop performance
Telianidis et al. 2014[26] *J Electromyog Kinesiology*	- 30 ACLR (17±2 mo surgery) - 30 healthy controls	- Submaximal isometric knee extension (60°) cyclical matching task, 5-30% MVIC - Quad & Hamstring EMG (VM, VL, RF, ST, & BF)	- Root mean square error (RMSE), torque vs target. ↑RMSE = ↓Control	- ↑RMSE in ACLR vs control. - Mod correlations: ↑RMSE & ↑ST activation ↑RMSE & ↑BF activation
Goetschius et al. 2015[17] *J Ortho Research*	- 32 ACLR (45.1±37.4 mo postop) - 32 Healthy controls	- Max isometric knee extension (90°) - 30-minutes exercise protocol	- Coefficient of variation (CV) - ΔCV = change in CV from baseline to post-exercise. ↑CV = ↓Control	- ↑CV in ACLR vs control at baseline. - ↑CV in ACLR vs control post-exercise. - ↑ΔCV in ACLR vs control.
Goetschius et al. 2015[16] *Unpub*	- 53 ACLR (44.1±29.9 mo postop) - 55 Healthy controls	- Max isometric knee extension (90°) - Subjective knee function (IKDC)	- Coefficient of variation (CV) ↑CV = ↓Control	- ↑CV in ACLR vs control *In ACLR participants - Weak-mod corr between ↑CV & ↓IKDC score
ACL Deficient				
Bryant et al. 2009[56] *J Bone Joint Surgery*	- 13 unilateral, ACL-D (75.6±72.4 mo injury) - 33 healthy controls	- Max isokinetic exten/flex (180°/s) - Hamstring EMG (ST & BF) - Timed SL hopping task	- Mean instantaneous frequency (wavelet transform). ↑Instant freq = ↓Control	- ↑Instant freq in ACL-D vs control. *Combined w/ ACLR - Mod correlation ↑Instant freq & ↑HS activation - ↑Instant freq related to faster hop performance
Scurvydas et al. 2011[59] *Knee Surgery Sport Traum Arthroscopy*	- 13 unilateral, ACL-D (4.8 ± 2.2 weeks injury)	- Submaximal isometric knee extension (90° & 60°) at 20% MVIC.	- Coefficient of variation (CV) ↑CV = ↓Control - Permutation entropy (PE) ↑PE = less regular torque	- No difference in CV between ACL-D and contralateral knee at either joint angle. - ↑PE in contralateral knee compared to ACL-D

Table B-1 Continued: Quadriceps Force Control in Knee Pathology Literature Review

Pua et al. 2014[57] *Knee Surgery Sport Traum Arthroscopy*	- 87 unilateral ACL-D (scheduled for ACLR)	- Max isokinetic exten/flex (60°/s) - SL hop distance - 6m hop velocity	- Mean instantaneous frequency (wavelet transform). ↑Instant freq = ↓Control	- ↑Instant freq in ACL-D vs contralateral knee. - Mod correlations: ↑Instant freq & ↓Hop distance ↑Instant freq & ↓Hop velocity
Knee Osteoarthritis				
Hortobagyi et al. 2004[14] *Arthritis and Rheumatsim*	20 knee OA (KL 2+) 20 age-matched healthy	- Isometric (65°) and isokinetic concentric/eccentric (15°/s) knee extension matching 50N & 100N	- Standard deviation (SD) ↑SD = ↓Control - Mean absolute error (MAE) ↑MAE = ↓control	- ↑SD and ↑MAE during eccentric and concentric contractions in OA vs control. - No difference in isometric SD or MAE between groups.
Sorensen et al. 2011 *J Ortho Sport Physical Therapy*	41 knee OA >medial compartment degeneration	- Isometric (90°) knee extension matching 25N & 50N - Walking gait: peak Add moment (Nm/BW*Ht%)	- Standard deviation (SD) ↑SD = ↓control	- No significant correlations between peak add moment and SD at 25N or 50N. - SD did not predict peak add moment.
Smith et al. 2014[15] *J Arthroplasty*	13 knee OA (scheduled for TKA) 11 age-matched healthy	- Isometric (45°) and isokinetic concentric/eccentric (15°/s) knee extension matching 50% MVIC (45°)	- Coefficient of variation (CV) ↑CV = ↓control	- ↑SD and ↑MAE during concentric contractions in OA vs control.

Gamma-Loop Dysfunction & Knee Pathology

Impairments in quadriceps muscle function may occur secondary to underlying changes in neural pathways secondary to ACLR injury.[18] Changes in the discharge of sensory receptors in the damaged knee may alter excitability of multiple spinal and supraspinal pathways that contribute to activation of the quadriceps muscles.[18] One pathway that has been studied in the quadriceps is the gamma-loop, a spinal reflex circuit between gamma motorneurons, muscle spindles, and Ia afferent fibers, which acts to maintain accurate sensory information to the CNS and reflexive motorneuron excitability to muscle.[19] Normally, the gamma-loop plays an important role in alpha-gamma co-activation and regulating muscle stiffness.[20] Experiments using animal models demonstrated a reflexive neural response from gamma motorneurons and primary and secondary muscle spindle afferents of surrounding knee musculature (hamstring and gastrocnemius) during sinusoidal stretching of the ACL.[19] Researchers concluded that ACL afferents may have a reflexive link to activity of gamma motorneurons and muscle spindles, and therefore the ACL may play a role in muscle activation and stiffness regulation.[19]

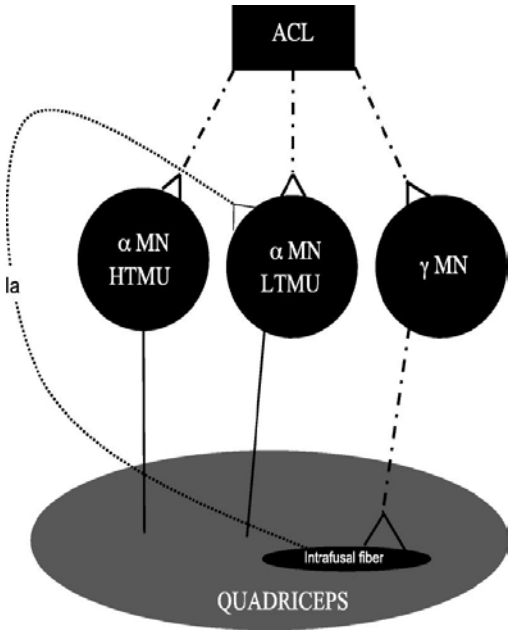


Figure B-2. Schematic diagram of the neural pathways between the ACL and gamma-loop (Palmieri-Smith 2009)[1]

Recent studies have used prolonged tendon vibration to investigate the potential effects of ACL reconstruction and other knee pathologies on muscle spindle and the gamma-loop. Researchers have observed an abnormal response to prolonged patellar

tendon vibration in ACLR[22,23] knees, as well as ACL-D[21] and OA[24] knees, when compared to healthy controls. A review of these studies is shown in the table below. Generally, healthy knees experienced a normal vibration-induced decline in peak knee extensor torque, while torque production in pathological knees would not change from baseline.[21-24] Due to repetitive stretching, prolonged vibration is thought to reduce Ia afferent signals from the muscle spindles of the muscle tissues be vibrated.[25] A reduction in Ia afferent signals would have an inhibitory effect on alpha motorneuron activity due to the excitatory reflexive circuit between the two pathways.[25] Researchers theorized that the abnormal response to vibration in ACLR knees may be due to disrupted gamma-loop pathway that interferes with the normal effects of prolonged vibration. Researchers coined that abnormal response to vibration, "gamma-loop dysfunction".[21,22,24]

This response to vibration has only been examined in patients during the early stages after ACLR, about 6-18 months after surgery. However, similar observation in chronic OA populations may suggest that this potential change in neural pathways may present in chronic ACLR patients as well. There is no current evidence regarding the relationship between quadriceps gamma-loop dysfunction and quadriceps muscle performance.

Table B-2: Gamma-Loop Dysfunction Literature Review Summary

Author	Subjects	Outcome	Vibration	Results
Konishi et al. 2002[21] *Med Sci Sport Exerc*	13 ACL-D 7 Healthy	- 90° MVIC - %-change in MVIC from baseline to post vibration.	-Infrapatellar tendon -20 min, 50 Hz, ~30N	- Significant difference in %-change in MVIC between groups (ES= 3.02 [1.88, 4.17]. - ACL-D= + change (- Healthy= - change.
Konishi et al. 2002[22] *Scan J Med Sci Sport*	10 ACLR (<6-mo.) 12 Healthy	- 90° MVIC - %-change in MVIC from baseline to post vibration.	-Infrapatellar tendon -20 min, 50 Hz, ~30N	- Significant decline in MVIC in healthy. No change in ACLR. - Significant difference in %-change in MVIC between groups (ES= 1.29 [0.37, 2.21]. - ACLR= -0.44% ± 7.87 - Healthy= -9.02% ± 5.46
Richardson et al 2006[23] *J Geriatric Phys Therapy*	14 ACLR: (6-12 mo.) 14 Healthy	- 75° MVIC - %-change in MVIC from baseline to post vibration	-Infrapatellar tendon -20 min, 50 Hz, ~30N	- Significant decline in MVIC in healthy. No change in ACLR. - ACLR= +4.7% - Healthy= -7.2%
Konishi et al. 2011 *Int J Sports Med*	9 ACLR (5-18 mo.) 10 Healthy	- 90° MVIC - %-change in MVIC from baseline to post vibration.	-Infrapatellar tendon -20 min, 50 Hz, ~30N	- Significant decline in MVIC in healthy. No change in ACLR. - Significant difference in %-change in MVIC between groups (ES= 2.78 [1.52, 4.05]. - ACLR= +4.7% ± 5.1 - Healthy= -9.5% ± 5.1
Rice et al 2011[24] *J Geriatric Phys Therapy*	15 Knee OA 15 Healthy	- 90° MVIC - %-change in MVIC from baseline to post vibration	-Infrapatellar tendon -20 min, 50 Hz, ~30N	- Significant decline in MVIC in healthy. No change in ACLR. - Significant difference in %-change in MVIC between groups (ES= 0.95 [0.20, 1.71]. - ACLR= -2.4% - Healthy= -8.2

APPENDIX C
Additional Methods

Table C-1. Overall Study Procedures

1. **Visit #1: Exercise & Sport Injury Lab B**
    a. Informed Consent
    b. Review Eligibility Criteria
    c. Participant Questionnaires
    d. Isometric Matching Task
    e. Isokinetic Matching Task
    f. Patellar Tendon Vibration Measure
2. **Visit #2: Exercise and Sport Injury Lab B & Gait Lab**
    - Visit #2 completed within 72 hours of visit #1
    a. Motion Capture: Walking & Jogging
    b. Isokinetic Strength Measure (flexion/extension)
    c. Isometric Fatigue Measure (flexion/extension)
    d. Single-leg Static Balance Measure
    e. Jump Landing Measure
    f. Single-leg Horizontal Hops Measure

Table C-2. Informed Consent

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Parents' or Guardians' Permission for Your Child to Be in a Research Study

Agreement of a Child to Be in a Research Study

In this form "you" means the child in the study *and* the parent or guardian.

- ✓ If you are the parent or guardian, you are being asked to give permission for your child to be in this study.
- ✓ If you are the child, you are being asked if you agree to be in this study.

In this form "we" means the researchers and staff involved in running this study at the University of Virginia.

Participant's Name_____

Principal Investigator: Dr. Joseph M. Hart, PhD, ATC
210 Emmet St South
Charlottesville, VA 22902
(e) jmh3zf@virginia.edu
(p) 434-924-6187

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

Who is funding this study?

There is no external funding source for this study.

Why is this research being done?

The purpose of this study is to learn more about leg muscle function after ACL reconstruction surgery. We know that leg function may change after an ACL surgery. The goal of this study is to determine whether the levels of muscle function or the quality of leg function may help predict how well someone will do after a surgery. Overall we hope to get information that may improve health care and quality of life for patients.

You are being asked to be in this study because:

1. You have had an ACL reconstruction surgery.
2. You are a knee-healthy individual with no history of major leg injury or surgery.

Up to 207 people will be in this study at UVA.

What will happen if you are in the study?

If you agree to be in this study, you will sign this consent form before any study related procedures take place.

We will then review your medical history relating to your ACL reconstruction surgery, rehabilitation, and current activity levels to make sure it is safe for you to participate.

STUDY PROCEDURES

This study involved 2 visits to UVA's Exercise and Sport Injury Laboratory with an optional 3rd visit for 20 participants.

- **Visit #1** will include measures of thigh muscle function. All measures will involve you sitting in a chair and either kicking out or pulling back your leg. For some measures you will try to kick or pull as hard as you can and for some measures you will try to match a line on a screen. One measure will involve placing a vibration device on the front of your knee. You will also be asked to fill out questionnaires about your knee and activity.
- **Visit #2** will include measures of how you hop, balance, walk, run, and land. We will ask you to hop for a distance on one leg, balance on one leg, and we will film your legs while you land after jumping from a short box. We will also ask you to walk and run on a treadmill and jump from a short box while specialized cameras film sensors on your legs.
- **Visit #3** will be an optional visit offered to some participants. This visit will include repeated measures of three of the thigh muscle measures from visit #1.
- **The procedures for each visit and measure are detailed below:**

Visit #1 (about 90 minutes)

1. ***Vibration Measure*** *(about 30 minutes)*
   - You will be asked to sit in a stationary chair with your knees bent at 90 degrees (a right angle).
   - Your hips will be secured with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device that will measure how much force you can produce.

- You will be asked to kick your leg out as hard as you can and hold for 3-seconds. This will be performed 3 times with rest in between.
- A small vibrating device will be placed against the front your knee. This device will vibrate against your knee and may make your thigh muscle shake a little. This will be done for 20 minutes while you sit in the stationary chair.
- After, you will be asked to kick your leg out as hard as you can and hold for 3-seconds again. This will be performed 3 times with rest in between.

2. ***Questionnaires*** *(about 10 minutes)*
   1. You will be asked to complete the following questionnaires below to best of your ability. *International Knee Documentation Committee (IKDC) Subjective Knee Evolution Form*- Asks about knee-related pain and difficulty with daily activities and exercise.
   2. *Knee Injury and Osteoarthritis Outcome Score (KOOS)*- Asks about knee-related pain and difficulty with daily activities and exercise.
   3. *Tegner Activity Scale*- Asks about physical activity level before and after your surgery.
   4. *Godin Leisure-time Exercise Questionnaire*- Asks about your current weekly physical activity.
   5. *Tampa Scale for Kinesiophobia*- Asks about your fear related to physical activity.

3. ***Force Matching*** *(about 10 minutes)*
   - You will be asked to sit in a stationary chair with your knees are bent at 90 degrees (a right angle).
   - Your hips will be secured with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device that will measure how much force you can produce.
   - For this test you will be kicking out to try and match a steady muscle force intensity that is shown on a screen in front of you. There will be two lines, one line will represent how hard you are kicking out and one line will represent the target goal you are trying to reach.
   - You will try and match forces at 25%, 50%, 75%, and 100% of your maximum contraction.
   - This will be performed on both legs, starting with your uninjured or non-dominant leg.

4. ***Force Tracking*** *(about 10 minutes)*
   - You will be asked to sit in a stationary chair with your knees bent at 90 degrees (a right angle).
   - Your hips will be secured with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device that will measure how much force you can produce.
   - For this test you will be kicking out to try and match a rising and falling muscle force intensity that is shown on a screen in front of you. There will be two lines, one line will represent how hard you are kicking out and one line will represent the target goal you are trying to reach.
   - The forces you are matching will range from 5-50% of your maximum contraction.
   - This will be performed on both legs, starting with your uninjured or non-dominant leg.
   -

5. ***Isokinetic Strength*** *(about 20 minutes)*
   - You will be asked to sit in a stationary chair with your knees bent at 90 degrees (a right angle).

- Your hips will be secured with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device which will measure how much force you can produce.
- You will be asked to kick out and pull back your leg 8 times. This will be repeated at two different levels of resistance.
- You may complete this trial as fast or as slowly as you choose.
- You will be asked to complete one trial at each level of resistance.
- This will be performed on both legs, starting with your uninjured or non-dominant leg.

6. ***Isometric Strength and Fatigue*** *(about 10 minutes)*
   - You will be seated in a stationary chair. The chair has handles on each side.
   - Your hips will be secured with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device designed to measure how much force you can produce.
   - You will be asked to kick out as hard as you can several times in order to estimate the most force you can produce. We will ask you to do this three times. You will rest for 2 minutes between each time.
   - You will then be asked to kick out at your maximum effort and hold your leg out for 30 seconds to measure how quickly your muscles become tired, also called motor fatigue. We will ask you to try to keep the same amount of force for as long as you can.
   - This will be performed on both legs, starting with your uninjured or non-dominant leg.

Visit #2 (about 90 minutes)

1. ***Single-Leg Balance*** *(about 10 minutes)*
   - We will ask you to stand with both legs on a force plate
   - Once balanced, we will ask you to pick one leg up, and balance on the other with your eyes closed. Each trial will last for 10 seconds. You will do this three times on each leg.

2. ***Jump-Landing*** *(about 5 minutes)*
   - You will be asked to stand on a raised platform (about 12 inches high)
   - You will then be asked to step down, land, then jump straight up.
   - We will ask you to do this three times
   - Video cameras will be used to record this activity from the front and side views.

3. ***Single-leg Hops*** *(about 15 minutes)*
   - You will then be asked to hop as far as you can on each leg multiple times in different directions.
   - The distance you hop will be measured along a tape measure.
   - We will also ask you to hop as quickly as possible over a distance of about 20 feet.
   - You will be given practice hop trials in order to practice before testing begins.
   - Once testing begins, three hop trials will be measured for each hop test.
   - This will be performed on both legs, starting with your uninjured or non-dominant leg.

4. ***Motion Analysis*** *(about 60 minutes)*

- *Small, white reflective markers will be taped to your legs and hips using double-sided adhesive tape.*
- *Specialty cameras will recorder the markers to record your leg movement.*
- *You will be asked to walk and jog on a treadmill at comfortable self-selected paces.*
- *You will be asked to jump off a 30 cm box onto a force plate in the ground and then jump as high as they are comfortable and land.*

Visit #3 (approximately 50 minutes)
This visit will be optional for 20 participants to ensure the stability of three of our assessments. You will repeat the 1) Vibration Measure, 2) Force Matching, and 3) Force tracking tests.

Study Schedule

	Visit 1	Visit 2	Visit 3 (optional)
Study Week		*Within 2-7 days of Visit 1*	*One week after Visit 1*
Informed Consent	X		
Review study eligibility	X		
Medical History	X		
Vibration Measure	X		X
Questionnaires	X		
Force Matching/Tracking	X		X
Muscle Strength/Endurance	X		
Balance, Landing, Hopping		X	
Motion Analysis		X	

WHAT ARE YOUR AND YOUR PARENT/LEGAL GUARDIAN'S RESPONSIBILITIES IN THE STUDY?
You and your parent/legal guardian have certain responsibilities to help ensure your safety.

These responsibilities are listed below:
- Your parent/legal guardian must bring you to each study visit.
- You and your parent/legal guardian must be completely truthful about your health history.
- Follow all instructions given.
- You or your parent/legal guardian should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.

How long will this study take?
Your part in this study will require 2 study visits over a 2-7 days. Each visit will last about 90 minutes. An extra 3rd visit will be offered for 20 participants.

If you want to know about the results before the study is done:
During the study you are having an investigational test done. The purpose of the test is NOT to diagnose any disease or abnormality you may have. Because the test is investigational there is no way for the study leader to understand if the results are "normal" or "abnormal".
However, IF any test results are concerning, your study leader will let you know.
In addition, as the research moves forward, your study leader will keep you informed of any new findings about the research itself that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

Could you be helped by being in this study?
You will not benefit from being in this study. However the information researchers get from this study may help others in the future.

What are the risks of being in this study?
Participation in this study includes the risk for minor knee and/or muscle soreness during or following participation. This soreness is similar to what you might experience during or following light physical activity. There is also a risk for falling if you lose your balance during the hopping tasks.

What are your other choices if you do not join this study?
You do not have to be in this study to be treated for your illness or condition.
If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?
You will be paid $20.00 for finishing Visit #1 and $20.00 for finishing Visit #2. If you complete Visit #3, you will be paid $10.00. All payment will be debit gift cards provided immediately following your visit.

Will being in this study cost you any money?
All of the procedures in this study will be provided at no cost to you or your health insurance. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?
If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you

receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?
You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study.

If you decide to stop being in the study, we will ask you to please contact the study coordinator you have been in contact with or the principle investigator, Dr. Joseph Hart.

How will your personal information be shared?
The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:
- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers.

Who will see your private information?
- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- Tax reporting offices (if you are paid for being in the study)

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

What if you sign the form but then decide you don't want your private information shared?
You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be

in the study. The researchers will still use information about you that was collected before you ended your participation.

Please contact the researchers listed below to:
- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Dr. Joseph M. Hart, PhD, ATC
210 Emmet St South
Charlottesville, VA 22902
(e) jmh3zf@virginia.edu
(p) 434-924-6187

What if you have a concern about this study?
You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908
Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Assent from Child

Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

Person Obtaining Assent of the Child (less than 18 years of age)

Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

By signing below you confirm that the study has been explained to the child (less than 18 years of age), all questions have been answered and the child has voluntarily agreed to participate.

PERSON OBTAINING ASSENT (SIGNATURE)	PERSON OBTAINING ASSENT (PRINT)	DATE

Parental/ Guardian Permission

By signing below you confirm you have the legal authority to sign for this child.

PARENT/GUARDIAN (SIGNATURE)	PARENT/GUARDIAN (PRINT NAME)	DATE

Person Obtaining Parental/Guardian Permission

By signing below you confirm that you have fully explained this study to the parent/guardian, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING PARENTAL/ GUARDIAN PERMISSION (SIGNATURE)	PERSON OBTAINING PARENTAL/GUARDIAN PERMISSION (PRINT NAME)	DATE

Consent from Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

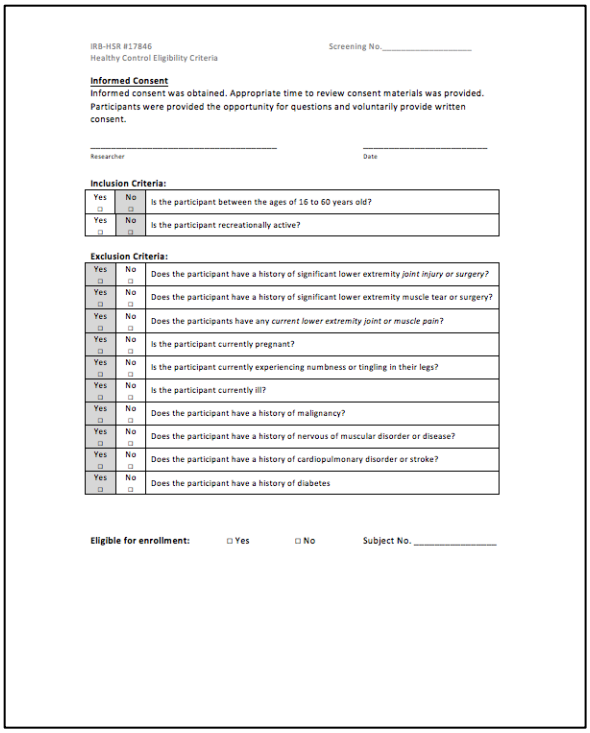
I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

- ☐ Subject
- ☐ Parent(s)/Guardian of the subject
- ☐ Subject's surrogate

IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Table C-3. Eligibility Criteria Review



IRB-HSR #17846 Screening No._____
Healthy Control Eligibility Criteria

Informed Consent
Informed consent was obtained. Appropriate time to review consent materials was provided. Participants were provided the opportunity for questions and voluntarily provide written consent.

_____ _____
Researcher Date

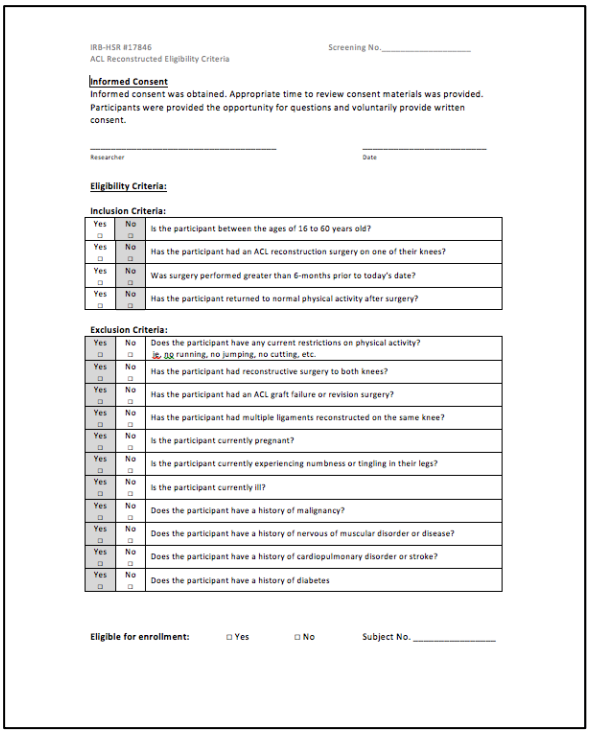
Inclusion Criteria:

Yes ☐	No ☐	Is the participant between the ages of 16 to 60 years old?
Yes ☐	No ☐	Is the participant recreationally active?

Exclusion Criteria:

Yes ☐	No ☐	Does the participant have a history of significant lower extremity *joint injury or surgery?*
Yes ☐	No ☐	Does the participant have a history of significant lower extremity muscle tear or surgery?
Yes ☐	No ☐	Does the participants have any *current lower extremity joint or muscle pain?*
Yes ☐	No ☐	Is the participant currently pregnant?
Yes ☐	No ☐	Is the participant currently experiencing numbness or tingling in their legs?
Yes ☐	No ☐	Is the participant currently ill?
Yes ☐	No ☐	Does the participant have a history of malignancy?
Yes ☐	No ☐	Does the participant have a history of nervous of muscular disorder or disease?
Yes ☐	No ☐	Does the participant have a history of cardiopulmonary disorder or stroke?
Yes ☐	No ☐	Does the participant have a history of diabetes

Eligible for enrollment: ☐ Yes ☐ No Subject No. _____



IRB-HSR #17846 Screening No._____
ACL Reconstructed Eligibility Criteria

Informed Consent
Informed consent was obtained. Appropriate time to review consent materials was provided. Participants were provided the opportunity for questions and voluntarily provide written consent.

_____ _____
Researcher Date

Eligibility Criteria:

Inclusion Criteria:

Yes ☐	No ☐	Is the participant between the ages of 16 to 60 years old?
Yes ☐	No ☐	Has the participant had an ACL reconstruction surgery on one of their knees?
Yes ☐	No ☐	Was surgery performed greater than 6-months prior to today's date?
Yes ☐	No ☐	Has the participant returned to normal physical activity after surgery?

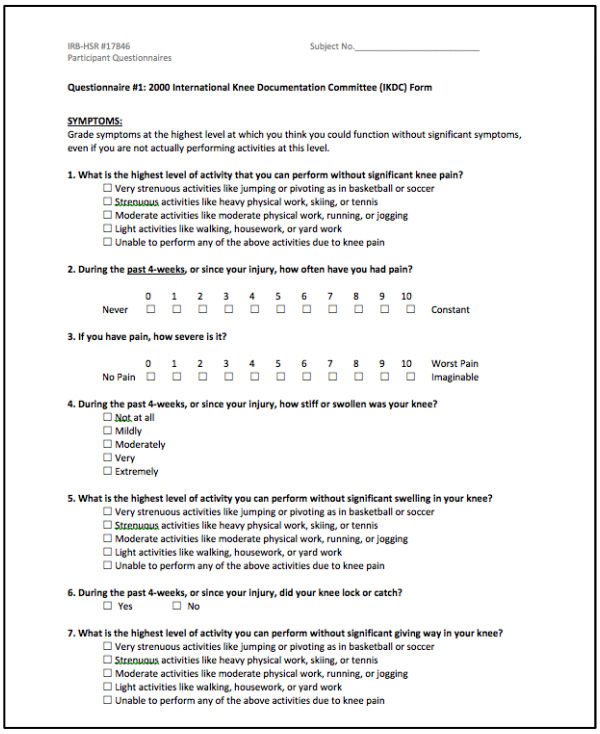
Exclusion Criteria:

Yes ☐	No ☐	Does the participant have any current restrictions on physical activity? ie. no running, no jumping, no cutting, etc.
Yes ☐	No ☐	Has the participant had reconstructive surgery to both knees?
Yes ☐	No ☐	Has the participant had an ACL graft failure or revision surgery?
Yes ☐	No ☐	Has the participant had multiple ligaments reconstructed on the same knee?
Yes ☐	No ☐	Is the participant currently pregnant?
Yes ☐	No ☐	Is the participant currently experiencing numbness or tingling in their legs?
Yes ☐	No ☐	Is the participant currently ill?
Yes ☐	No ☐	Does the participant have a history of malignancy?
Yes ☐	No ☐	Does the participant have a history of nervous of muscular disorder or disease?
Yes ☐	No ☐	Does the participant have a history of cardiopulmonary disorder or stroke?
Yes ☐	No ☐	Does the participant have a history of diabetes

Eligible for enrollment: ☐ Yes ☐ No Subject No. _____

Table C-4. Participant Questionnaires

International Knee Documentation Committee 2000 Form (IKDC)[60]



IRB-HSR #17846 Subject No._____
Participant Questionnaires

Questionnaire #1: 2000 International Knee Documentation Committee (IKDC) Form

SYMPTOMS:
Grade symptoms at the highest level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?
- ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
- ☐ Strenuous activities like heavy physical work, skiing, or tennis
- ☐ Moderate activities like moderate physical work, running, or jogging
- ☐ Light activities like walking, housework, or yard work
- ☐ Unable to perform any of the above activities due to knee pain

2. During the past 4-weeks, or since your injury, how often have you had pain?

	0	1	2	3	4	5	6	7	8	9	10	
Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Constant

3. If you have pain, how severe is it?

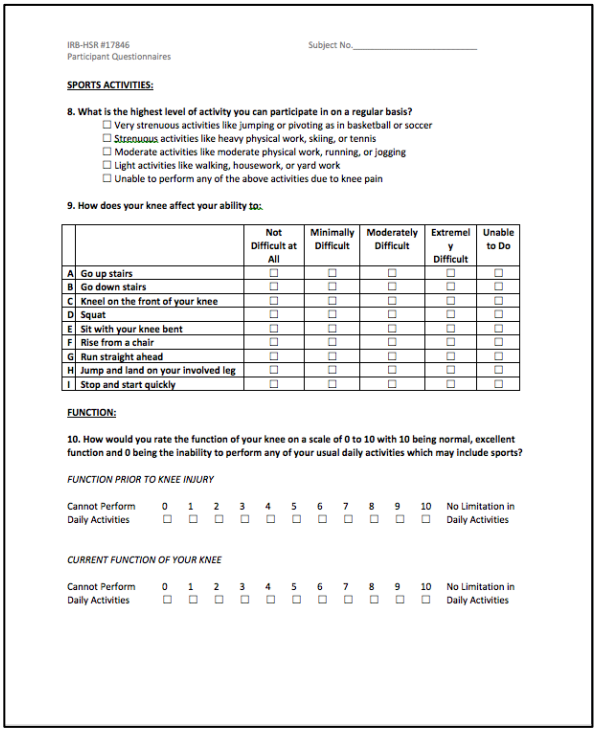
	0	1	2	3	4	5	6	7	8	9	10	
No Pain	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Worst Pain Imaginable

4. During the past 4-weeks, or since your injury, how stiff or swollen was your knee?
- ☐ Not at all
- ☐ Mildly
- ☐ Moderately
- ☐ Very
- ☐ Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?
- ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
- ☐ Strenuous activities like heavy physical work, skiing, or tennis
- ☐ Moderate activities like moderate physical work, running, or jogging
- ☐ Light activities like walking, housework, or yard work
- ☐ Unable to perform any of the above activities due to knee pain

6. During the past 4-weeks, or since your injury, did your knee lock or catch?
☐ Yes ☐ No

7. What is the highest level of activity you can perform without significant giving way in your knee?
- ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
- ☐ Strenuous activities like heavy physical work, skiing, or tennis
- ☐ Moderate activities like moderate physical work, running, or jogging
- ☐ Light activities like walking, housework, or yard work
- ☐ Unable to perform any of the above activities due to knee pain



IRB-HSR #17846 Subject No._____
Participant Questionnaires

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?
- ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
- ☐ Strenuous activities like heavy physical work, skiing, or tennis
- ☐ Moderate activities like moderate physical work, running, or jogging
- ☐ Light activities like walking, housework, or yard work
- ☐ Unable to perform any of the above activities due to knee pain

9. How does your knee affect your ability to:

		Not Difficult at All	Minimally Difficult	Moderately Difficult	Extremely Difficult	Unable to Do
A	Go up stairs	☐	☐	☐	☐	☐
B	Go down stairs	☐	☐	☐	☐	☐
C	Kneel on the front of your knee	☐	☐	☐	☐	☐
D	Squat	☐	☐	☐	☐	☐
E	Sit with your knee bent	☐	☐	☐	☐	☐
F	Rise from a chair	☐	☐	☐	☐	☐
G	Run straight ahead	☐	☐	☐	☐	☐
H	Jump and land on your involved leg	☐	☐	☐	☐	☐
I	Stop and start quickly	☐	☐	☐	☐	☐

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

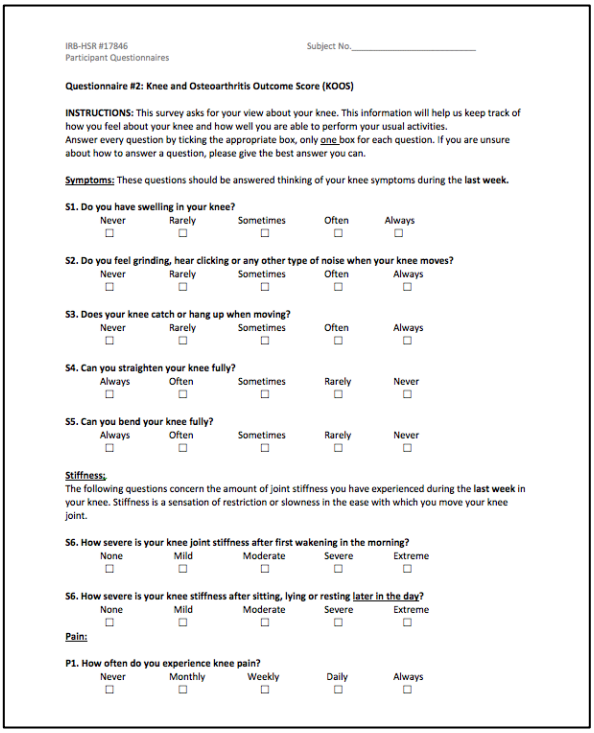
FUNCTION PRIOR TO KNEE INJURY

	0	1	2	3	4	5	6	7	8	9	10	
Cannot Perform Daily Activities	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	No Limitation in Daily Activities

CURRENT FUNCTION OF YOUR KNEE

	0	1	2	3	4	5	6	7	8	9	10	
Cannot Perform Daily Activities	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	No Limitation in Daily Activities

Knee Injury and Osteoarthritis Outcome Score (KOOS)[61]



IRB-HSR #17846 Subject No._____
Participant Questionnaires

Questionnaire #2: Knee and Osteoarthritis Outcome Score (KOOS)

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.
Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms: These questions should be answered thinking of your knee symptoms during the **last week.**

S1. Do you have swelling in your knee?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐

S3. Does your knee catch or hang up when moving?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐

S4. Can you straighten your knee fully?
Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never ☐

S5. Can you bend your knee fully?
Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never ☐

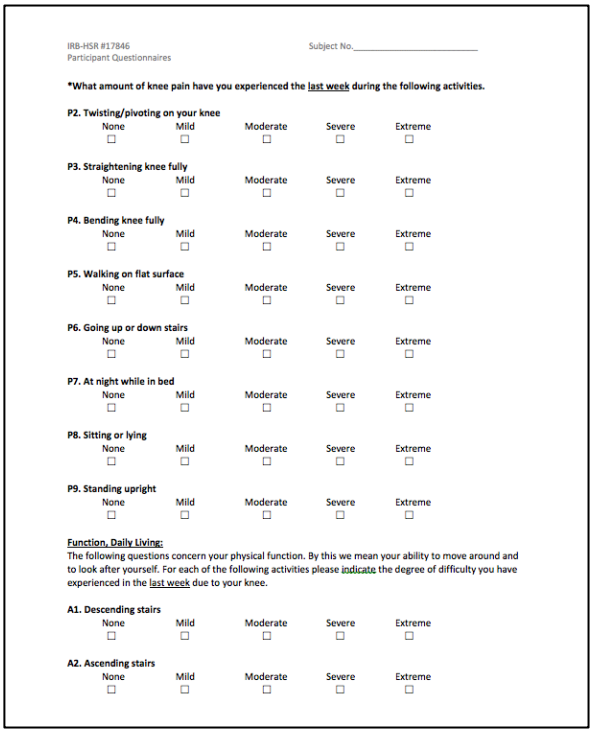
Stiffness:
The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

S6. How severe is your knee stiffness after sitting, lying or resting later in the day?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Pain:

P1. How often do you experience knee pain?
Never ☐ Monthly ☐ Weekly ☐ Daily ☐ Always ☐



IRB-HSR #17846 Subject No._____
Participant Questionnaires

***What amount of knee pain have you experienced the last week during the following activities.**

P2. Twisting/pivoting on your knee
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P3. Straightening knee fully
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P4. Bending knee fully
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P5. Walking on flat surface
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P6. Going up or down stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P7. At night while in bed
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P8. Sitting or lying
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

P9. Standing upright
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Function, Daily Living:
The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.

A1. Descending stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A2. Ascending stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Participant Questionnaires

Subject No._____

***For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.**

A3. Rising from sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A4. Standing
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A5. Bending to floor/pick up an object
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A6. Walking on flat surface
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A7. Getting in/out of car
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A8. Going shopping
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A9. Putting on socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A10. Rising from bed
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A11. Taking of socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A12. Lying in bed (turning over, maintaining knee position)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A13. Getting in/out of bath
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A14. Sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Participant Questionnaires

Subject No._____

A15. Getting on/off toilet
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

***For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.**

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A17. Light domestic duties (cooking, dusting, etc)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Function, sports and recreational activities:
The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the last week due to your knee.

SP1. Squatting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

SP2. Running
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

SP3. Jumping
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

SP4. Twisting/pivoting on your injured knee
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

SP5. Kneeling
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Participant Questionnaires

Subject No._____

Quality of Life:

Q1. How often are you aware of your knee problem?
Never ☐ Monthly ☐ Weekly ☐ Daily ☐ Constantly ☐

Q2. Have you modified your lifestyle to avoid potentially damaging activities to your knee?
Not at all ☐ Mildly ☐ Moderately ☐ Severely ☐ Totally ☐

Q3. How much are you troubled with lack of confidence in your knee?
Not at all ☐ Mildly ☐ Moderately ☐ Severely ☐ Extremely ☐

Q4. In general, how much difficulty do you have with your knee?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Tegner Activity Level Scale[62]

IRB-HSR #17846 Subject No._____
Participant Questionnaires

Questionnaire #3: Tegner Activity Level Scale

Please indicate in the spaces below the HIGHEST level of activity that you participated in BEFORE YOUR INJURY and the highest level you are able to participate in CURRENTLY.

BEFORE INJURY/SURGERY: Level:_____ **CURRENT:** Level:_____

Level 10	Competitive Sports – Soccer, Football, Rugby (national elite).
Level 9	Competitive Sports – Soccer, Football, Rugby (lower divisions). – Ice hockey, Wrestling, Gymnastics, Basketball.
Level 8	Competitive Sports – Racquetball, Squash or Badminton, Track and field athletics (jumping, etc.), Down-hill skiing.
Level 7	Competitive Sports – Tennis, Running, Motorcars speedway, Handball. Recreational Sports – Soccer, Football, Rugby, Ice hockey, Basketball, Squash, Racquetball, Running.
Level 6	Recreational Sports – Tennis, Badminton, Handball, Racquetball, Down-hill skiing, Jogging at least 5x per week.
Level 5	Work – Heavy labor (construction, etc.). Competitive Sports – Cycling, Cross-country skiing. Recreational Sports – Jogging on uneven ground at leas 2x per week.
Level 4	Work – Moderately heavy labor (eg. Truck driving, etc.).
Level 3	Work – Light labor (nursing, etc.).
Level 2	Work – Light labor Walking on uneven ground possible, but impossible to back pack or hike.
Level 1	Work – Sedentary (secretarial, etc.)
Level 0	Sick leave or disability pension because of knee problems

Godin Leisure-Time Exercise Scale[63]

IRB-HSR #17846 Subject No._____
Participant Questionnaires

Questionnaire #4: Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

STRENUOUS EXERCISE **(Heart Beats Rapidly)** Examples: running, jogging, hockey, football, soccer, squash, basketball, cross-country skiing, judo, roller skating, vigorous swimming, vigorous long distance cycling	Number of Times Per Week _____
MODERATE EXERCISE **(Not Exhausting)** Examples: fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing	Number of Times Per Week _____
MILD EXERCISE **(Minimal Effort)** Examples: yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking	Number of Times Per Week _____

2. During a typical 7-day period (1-week), how often to your engage in an regular activity long enough to work up a sweat (heart beats rapidly) during your leisure-time?

☐ Often ☐ Sometimes ☐ Never/Rarely

Tampa Scale for Kinesiophobia[64]

IRB-HSR #17846 Subject No._____
Participant Questionnaires

Questionnaire #5: Tampa Scale for Kinesiophobia (TSK)

	Check the box that best describes your belief for each statement below:	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
1.	I am afraid that I might injury myself if I exercise.	☐	☐	☐	☐
2.	If I were to try to overcome it, my pain would increase.	☐	☐	☐	☐
3.	My body is telling me I have something dangerously wrong.	☐	☐	☐	☐
4.	My pain would probably be relieved if I were to exercise.	☐	☐	☐	☐
5.	People are not taking my medical condition seriously enough.	☐	☐	☐	☐
6.	My accident has put my body at risk for the rest of my life.	☐	☐	☐	☐
7.	Pain always means I have injured my body.	☐	☐	☐	☐
8.	Just because something aggravates my pain does not mean it is dangerous.	☐	☐	☐	☐
9.	I am afraid that I might injure myself accidentally.	☐	☐	☐	☐
10.	Simply being careful that I do not make any unnecessary movements in the safest thing I can do to prevent my pain from worsening.	☐	☐	☐	☐
11.	I would not have this much pain if there were not something potentially dangerous going on in my body.	☐	☐	☐	☐
12.	Although my condition is painful, I would be better off if I were physically active.	☐	☐	☐	☐
13.	Pain lets me know when to stop exercising so that I do not injure myself.	☐	☐	☐	☐
14.	It is really not safe for a person with a condition like mine to be physically active.	☐	☐	☐	☐
15.	I cannot do all the things normal people do because it is too easy for me to get injured.	☐	☐	☐	☐
16.	Even though something is causing me a lot of pain, I do not think it is actually dangerous.	☐	☐	☐	☐
17.	No one should have to exercise when he/she is in pain.	☐	☐	☐	☐

Table C-5. Isometric Force-Matching Task Methods

1. **Instruments:**
   a. Biodex System III Dynamometer (Biodex Medical, Inc., Shirley, NY)
   b. Biopac Data Acquisition System (Biopac Systems, Inc., Goleta, CA)
   c. AcqKnowledge 4.2 Software (Biopac Systems, Inc., Goleta, CA)
2. **Biodex Set-up:**
   a. Turn on Biodex System III and select isometric mode
   b. Locate the remote access port: plug the 'torque' cable into channel 1 of the MP150 unit.
   c. Set the torque arm to 45 degrees using a handheld inclinometer.
   d. Set the Biodex chair backrest to 85 degrees.
3. **Participant Positioning:**
   a. Seated in Biodex chair, arms resting comfortably across chest.
   b. Hips & knees flexed to 85 and 45-degrees of flexion, respectively.
   c. Lateral joint line aligned with the dynamometer axis.
   d. Torque arm secured to distal lower leg just superior to malleoli.
   e. Restrain subject's waist using the lap belt.
4. **Maximal Volitional Isometric Contraction (MVIC):**
   a. Open file template "000_IsometricMatching_Left" or "000_IsometricMatching_Right"
   b. Instruct participant on "proper knee extension contraction technique":
      i. Focus on using only quadriceps muscles to kick-out.
      ii. Do not extend trunk or raise hips in during contraction.
      iii. Gradually increase contraction to desired intensity.
   c. Instruct participant to perform three 5-second maximal knee extension contractions with a maximal plateau.
   d. Calculate average MVIC (V) using the 'Mean' of the middle 3-seconds of each contraction.
5. **AcqKnowledge Setup:**
   a. *MP150* | *Setup Channels …* | *Calculations* Tab
      i. Select Channel "C1, % MVIC" | *Setup…*
         1. Edit "Old Units: Point 1" = MVIC value (V)
      ii. Select Channel "C3, 25% Absolute Error" | *Setup…*
         1. Replace ".99" in expression equation (below) with MVIC value
         2. "ABS(((.99*.25)*152.34)-C2)"
      iii. Select Channel "C4, 50% Absolute Error" | *Setup…*
         1. Replace ".99" in expression equation below with MVIC value
         2. "ABS(((.99*.50)*152.34)-C2)"
   b. Right-click y-axis on right.
      i. Set *Upper:* = 60 and Lower = -10
      ii. ☑ Apply to all channels for Upper and Lower
6. **Testing:**
   a. For each trial, participants will increase isometric knee extension until the red output line (representing contraction) reaches the green target line. Participants

will sustain contraction for 5-second while attempting to match red data output line to green target line for the full 5-seconds.

b. Target intensities will be at 25% and 50% of MVIC, designated by the green target lines, and performed in series with 30-seconds rest between each trial.
c. 1 practice series will be performed followed by 3 test series with 60-second rest between each series, for a total of 3 trials per target intensity.

7. Data Processing:

a. Coefficient of Variation:
   i. Open the "Torque Nm" window.
   ii. Identify the first 25% trial and highlight a 3-second epoch starting from the point 1-second after the participant first reaches the target line.
   iii. Calculate the standard deviation (Stddev) and mean (Mean) using the AcqKnowledge outputs.
   iv. Repeat for 3x trials for each target intensity. Calculate average standard deviation and mean.
   v. Calculate coefficient of variation using the formula below:

$$Coefficient\ of\ Variation\ (CV) = \frac{Standard\ deviation}{Mean} \times 100$$

   vi. Repeat steps ii-v for the 50% trials

a. Absolute Error
   i. Open the "25% Absolute Error" data window. Highlight a 3-second epoch start from the point 1-second after the participant first reaches the target line.
   ii. Calculate the 'Mean' using the AcqKnowledge outputs.
   iii. Repeat for 3x trials for each target intensity. Calculate average 25% absolute error for the 3 trials.
   iv. Repeats steps i-iii for the in the "50% Absolute Error" data window.

Table C-6. Isokinetic Force-Matching Task Methods

1. **Instruments:**
   a. Biodex System III Dynamometer (Biodex Medical, Inc., Shirley, NY)
   b. Biopac Data Acquisition System (Biopac Systems, Inc., Goleta, CA)
   c. AcqKnowledge 4.2 Software (Biopac Systems, Inc., Goleta, CA)
2. **Biodex Set-up:**
   a. Turn on Biodex System III
   b. Locate the remote access port: plug the 'torque' cable into channel 1 and the 'position' cable into channel 2 of the MP150 unit.
   c. Set the torque arm to 90 degrees using a handheld inclinometer.
   d. Using *Panel Mode* set Biodex to the following specifications
      i. *Range of motion:* Towards = 65 degrees, Away = 15 degrees
      ii. *Mode:* Isokinetic
      iii. *Contraction:* Away = Concentric, Towards= Eccentric
      iv. *Speed:* Away= 10 degrees/Second, Towards= 10 degrees/second
      v. *Torque*: Eccentric= 50 ft lbs
3. **Participant Positioning:**
   a. Seated in Biodex chair, arms resting comfortably across chest.
   b. Hips flexed to 85-degrees of flexion.
   c. Lateral joint line aligned with the dynamometer axis.
   d. Torque arm secured to distal lower leg just superior to malleoli.
   e. Restrain subject's waist using the lap belt.
4. **AcqKnowledge Setup:**
   a. Open AcqKnowledge file: "000_IsokineticForceMatching_Right" or "000_IsokineticForceMatching_Left"
   b. Select: *MP150* | *Setup Channels…*| *Calculations tab*
      i. Select: Channel "C1, % MVIC" | *Setup…*
         1. Edit: Old Units, Point 1 = MVIC value (V) (from isometric trials)
      ii. Select Channel "C3, 25% Absolute Error" | *Setup…*
         1. Replace ".99" in expression equation (below) with MVIC value
         2. "ABS(((.99*.25)*152.34)-C2)"
5. **Testing:**
   a. Instruct patient on task and allow opportunity familiarize with concentric/eccentric contractions.
   b. Participant will perform alternating concentric and eccentric contractions while attempting to match 25% target line through out all contractions.
   c. Participants will perform two sets of practice trials with a series of 4 consecutive concentric/eccentric contractions with 1:00 min rest between trials.
   d. Test trials will include another set of 4 concentric/eccentric contractions.
8. **Data Processing:**
   a. Coefficient of Variation:
      i. Open the "Torque Nm" and "Position (degrees)" windows.
      ii. Identify the 4 concentric and 4 eccentric contractions using the position output for reference. The 1st concentric and eccentric contractions will not be used for analysis

iii. Highlight the middle 3-second epoch of the second contraction.
iv. Calculate the standard deviation (Stddev) and mean (Mean) using the AcqKnowledge outputs.
v. Repeat for each concentric and eccentric trial. Calculate the average standard deviation and mean for the 3 concentric and 3 eccentric trials
vi. Calculate coefficient of variation using the formula below:

$$Coefficient\ of\ Variation\ (CV) = \frac{Standard\ deviation}{Mean} \times 100$$

b. Absolute Error
   i. Open the "25% Absolute Error" and "Position (degrees)" windows.
   ii. Identify the 4 concentric and 4 eccentric contractions using the position output for reference. The 1st concentric and eccentric contractions will not be used for analysis.
   iii. Highlight the middle 3-second epoch of the second contractions.
   iv. Calculate 'Mean' using the AcqKnowledge outputs.
   v. Repeat for each concentric and eccentric trial. Calculate the average standard deviation and mean for the 3 concentric and 3 eccentric trials

Table C-7. Patellar Tendon Vibration Methods

1. **Instruments:**
   a. Biodex System III Dynamometer (Biodex Medical, Inc., Shirley, NY)
   b. Biopac Data Acquisition System (Biopac Systems, Inc., Goleta, CA)
   c. AcqKnowledge 4.2 Software (Biopac Systems, Inc., Goleta, CA)
   d. Deep Tissue Therapeutic Massager (Wahl Clipper Corp., Sterling, IL)
2. **Biodex Set-up:**
   a. Turn on Biodex System III and select isometric mode
   b. Locate the remote access port from the back of the Biodex system and plug the 'torque' cable into channel 1 of the MP150 unit.
   c. Set the torque arm to 90 degrees using a handheld inclinometer.
   d. Set the Biodex chair backrest to 85 degrees.
3. **Participant Positioning:**
   a. Seated in Biodex chair, arms resting comfortably across chest.
   b. Hips & knees flexed to 85 and 90-degrees of flexion, respectively.
   c. Lateral joint line aligned with the dynamometer axis.
   d. Torque arm secured to distal lower leg just superior to malleoli and locked at 90 degrees.
   e. Restrain subject's waist using the lap belt.
4. **Knee Extension Torque:**
   a. Open the Acqknowledge 4.2 file template:
      i. "000_Vibration_Left" or "000_Vibration_Right"
   b. Instruct participant on "proper knee extension contraction technique":
      i. Focus on using only quadriceps muscles to kick-out.
      ii. Do not extend trunk or raise hips in during contraction.
      iii. Gradually increase contraction to desired intensity.
   c. Perform warm-up contraction at subjective 25%, 50%, and 75% of MVIC.
   d. Perform minimum of two MVIC to confirm proper contraction technique.
   e. Perform 3 x 5-second MVIC contractions with 30-seconds rest between
   f. Post-vibration:
      i. Review proper knee extension contraction technique
      ii. Repeat 3 x 5-second MVIC contractions with 30-seconds rest between immediately following vibration protocol
5. **Vibration Protocol:**
   a. Position vibrator and stand so that applicator tip is resting against and aligned with the mid-substance of patella tendon.
   b. Using a handheld dynamometer, apply approximately 30 N of pressure to the lower crossbeam of the vibrator stand so the tip of the vibrator is applied to the tendon at the same force. Place a 25lb dumbbell on the lower portion of the stand to sustain the position and force application.
   c. Turn the dial on the vibrator to the white mark (= 50 Hz) and ensure the applicator is still proper alignment. Periodically reassess throughout protocol.
   d. Begin timer for 20 minutes of continuous vibration.
   e. Slide vibrator away from participant and Biodex and begin post-vibration knee extension torque measure.

6. **Processing:**
   a. Using the “Max” outcome in AcqKnowledge, calculate the peak torque (1 V = 152.34 Nm) for the 3x baseline and 3x post-vibration knee extension MVIC.
   b. Calculate the mean peak torque at baseline and post-exercise using the 3 trials, then calculate the percent change using the means and formula below:

$$Percent\ Change = \frac{Post\text{-}vibration - Baseline}{Baseline} \times 100$$

Table C-8. Gait Motion Capture Methods

1. **Equipment:**
    a. 6 Vicon Bonita Cameras (Vicon, Oxford, UK)
    b. Bertec Instrumented Treadmill (Bertec Corporation, Columbus, OH)
    c. Vicon Nexus Software (Vicon, Oxford, UK)
    d. Motion Monitor Software (Innovative Sports Training, Inc., Chicago, IL)
2. **Vicon Nexus:**
    a. Calibrate cameras
    b. Open new subject using "17846_Template1"
    c. Capture 1-second static trial → complete static calibration
    d. Capture 1-second static trial + 3-second marching trial → complete functional calibration
    e. Set to "Live Mode"
3. **Marker Set-up**
    a. Using double-sided tape and athletic tape secure 21 markers.
        i. Hips: *Sacral Cluster*: 1) Cluster_S, 2) Cluster_R, 3) Cluster_I, 4) Cluster_L, 5) L_ASIS, 6) R_ASIS.
        ii. Left Limb: 1) L_Heel, 2) L_Toe, 3) L_LatMal, 4) L_Shank, 5) L_Knee, 6) L_MidThigh 7) L_ProxThigh
        iii. Right Limb: 1) R_Heel, 2) R_Toe, 3) R_Dorsum, 4) R_LatMal, 5) R_Shank, 6) R_Knee, 7) R_MidThigh, 8) R_ProxThigh.
    b. Using calipers, measure knee joint and ankle joint width.
4. **Motion Monitor Set-up**
    a. Open preference file, "17846_Setup-Markers".
    b. Confirm markers and virtual sensor assignment
        i. Administration | Edit Sensor Assignments
            1. Sensor 1: Cluster_S, Cluster_R, Cluster_I, Cluster L
            2. Sensor 2: L_MidThigh, L_ProxThigh, L_Knee
            3. Sensor 3: L_Knee, L_Shank, L_LatMal
            4. Sensor 4: L_Heel, L_LatMal, L_Toe
            5. Sensor 2: R_MidThigh, R_ProxThigh, R_Knee
            6. Sensor 3: R_Knee, R_Shank, R_LatMal
            7. Sensor 4: R_Heel, R_LatMal, R_Toe, R_Dorsum
    c. Setup virtual sensor
        i. Setup | Setup virtual sensors
    d. Calibrate force plates
        i. Press buttons on each force plate box
        ii. Administration | Edit Force Plates | Configure | Calibrate (0 & 1)
    e. Setup subject sensors
        i. Setup | Setup subject sensors | Fixed markers
            1. Use forceplate for weight, Enter height (cm)
            2. Enter joint offsets = 1/2 joint widths (m)
            3. Test markers

f. Set Capture Parameters
    i. Setup | Edit Capture Parameters
        1. Edit name for files save
        2. 3-second capture times, End trigger: after 3-second

5. Treadmill

a. Turn power switch on and press flashing button.
b. Open “Bertec Treadmill” software.
c. Standard walking speed = 1.34m/s
d. Standard jogging speed = 2.68 m/s

6. Data Collection

a. Allow 3:00 of walking/jogging at selected speed for familiarization
b. Record 16 trials of: 1) walking standard speed, 2) walking self-selected speed, 3) jogging standard speed, 4) jogging self-selected speed.
c. Check data after each activity before moving on to next.

7. Data Processing

a. Open preference file “17846_Walk_Left” or “17846_Walk_Right”
b. View data for outlier/error data
    i. Analyze | Data Reduction
    ii. Select all 16 trials for participant
    iii. Visualize graphs for outlier/error trials and not trials numbers.
c. Analyze data
    i. Analyze | Data Reduction
    ii. Select the 10 trials you wish to include
    iii. Open file in excel.

Table C-9. Isokinetic Knee Extension & Flexion Strength Methods

1. **Instruments:**
   - **a.** Biodex System III Dynamometer (Biodex Medical, Inc., Shirley, NY)
   - **b.** Biodex System III Software (Biodex Medical, Inc., Shirley, NY)
2. **Biodex Setup**
   - **a.** Set Biodex to "Computer Control"
   - **b.** Open Biodex Software.
   - **c.** Input new patient information
   - **d.** Select "ACLR ORTHO PROTOCOL" as the protocol.
   - **e.** Select limb side.
   - **f.** Select the "ROM" icon.
     - **i.** Instruct participant to fully extend knee: Set "AWAY limit"
     - **ii.** Instruct participant to fully flex knee: Set "TOWARD limit"
   - **g.** Set reference angle to 90 degrees of flexion
   - **h.** Move participant's knee to 15 degrees of flexion, Set "Weight"
3. **Participant Positioning:**
   - a. Seated in Biodex chair, arms resting comfortably across chest.
   - b. Hips flexed to 85-degrees of flexion.
   - c. Lateral joint line aligned with the dynamometer axis.
   - d. Torque arm secured to distal lower leg just superior to malleoli.
   - e. Restrain subject's waist using the lap belt.
4. **Testing:**
   - a. Select "Go", dynamometer will engage. Allow participant opportunity to extend and flex knee familiarize themselves with the first contraction speed = 90 degrees/second.
   - b. When ready, position knee at 90 degrees flexion until green "Go" light is visible.
   - c. Instruct participant to extend and flex knee as hard and as fast as possible against the resistance. Participants will complete 8 consecutive extension/flexion contractions.
   - d. Screen will countdown 45 seconds of rest, the dynamometer will engage at second contraction speed = 180 degrees/second.
   - e. Allow participant opportunity to familiarize with new speed.
   - f. Repeat steps b-c at new speed.
5. **Data Processing:**
   - a. Under Patient tab, find patient and select limb results you wish to view.
   - b. Select report
   - c. Select metric and comprehensive.
   - d. Select print preview to view results.

Table C-10. Isometric Knee Extension & Flexion Fatigue Methods

1. **Instruments:**
   e. Biodex System III Dynamometer (Biodex Medical, Inc., Shirley, NY)
   f. Biopac Data Acquisition System (Biopac Systems, Inc., Goleta, CA)
   g. AcqKnowledge 4.2 Software (Biopac Systems, Inc., Goleta, CA)
2. **Biodex Set-up:**
   e. Turn on Biodex System III and select isometric mode
   f. Locate the remote access port from the back of the Biodex system and plug the 'torque' cable into channel 1 of the MP150 unit.
   g. Set the torque arm to 90 degrees using a handheld inclinometer.
   h. Set the Biodex chair backrest to 85 degrees.
3. **Participant Positioning:**
   a. Seated in Biodex chair, arms resting comfortably across chest.
   b. Hips & knees flexed to 85 and 90-degrees of flexion, respectively.
   c. Lateral joint line aligned with the dynamometer axis.
   d. Torque arm secured to distal lower leg just superior to malleoli and locked at 90 degrees.
   e. Restrain subject's waist using the lap belt.
4. **Testing:**
   a. Open "000_Fatigue_Exten_L", "000_Fatigue_Exten_R", "000_Fatigue_Flex_L", or "000_Fatigue_Flex_R"
   b. Instruct patient to perform knee extension or flexion MVIC contraction and hold for 30-seconds.
   c. Start data collection when participant has reached max contraction.
   d. Do not provide visual or verbal feedback or encouragement.
5. **Data Processing:**
   a. View results window
   b. Move cursor to last value of "Result" output.
   c. Record the "Value" = % decline.

Table C-11. Single Leg Static Balance Methods

1. **Instruments:**
   a. Accusway Force Plate (AMTI, Watertown, MA)
   b. Balance Clinic Software (AMTI, Watertown, MA)
2. **Equipment Setup:**
   a. Locate level surface on floor and place force plate.
   b. Plug force plate into the 'A' port of the PJB-101 box.
   c. Plug labtop into the 'RS-232' port of the PJB-101 box.
   d. Plug PJB-101 and laptop power sources into local wall outlet.
   e. "Zero" the force plate by pressing the button in the PJB-101 box with no mass on the plate.
3. **Balance Clinic Setup:**
   a. In the lower menu items: Select → *Setup*
      i. Under *Data Folder:* Select → *Browse*
      ii. Locate the folder to save data. Highlight and select → *Open*
      iii. Under *Protocol:* Select → *Browse*
      iv. Locate "LEAP.pro". Highlight and select → *Open*
      v. Select → *OK*
   b. Under *Test Sequence:* Select → *Zero Platform*
4. **Participant Positioning:**
   a. Align test limb foot with the center of the force plate.
   b. Flex hip and knee to ~30° and ~45° flexion, respectively.
   c. Place hands on hips and close eyes.
5. **Testing:**
   a. Ensure participant is in testing position.
   b. Select → *Acquire.* COP path motion should display in screen to right.
   c. System will signal when 10 seconds are complete.
   d. Select → *Save Data*. Save file by standardized names.
6. **Failed Trial:**
   a. Eyes open or hands off hips.
   b. Stance foot position deviates.
   c. Non-stance limb touches floor/force plate or stance limb.
7. **Data Analysis:**
   a. In the lower menu items: Select → *Load*
      i. Locate the trial file. Highlight and select → *Open*
   b. Under *Test Sequence:* Select → *Analyze*
   c. Identify the outcomes of interest in the scroll window.
   d. Repeat steps a-c for each trial.

Table C-12. Jump Landing Methods

1. **Instruments:**
    a. 30 cm Box
    b. 2 x HD Camcorders, Vixia HF R42 (Canon USA, Inc., Melville, NY)
2. **Equipment Setup:**
    a. Place box at 50% participant body height behind landing target
    b. Position Cameras:
        i. 48" from ground
        ii. 136" from center of landing target (1 sagittal, 1 frontal)
3. **Participant Positioning**
    a. Standing on top of box facing landing target
    b. Toes at the anterior edge of box
    c. Feet shoulder width apart
4. **Testing:**
    a. Instruct participant to leap off box, land on target, and complete a maximum vertical jump. Jumping landing should be performed in one fluid motion.
    b. Allow participant to perform at least 2 practice trials or until comfortable.
    c. Turn on cameras
    d. Instruct participant to perform 3 consecutive trials.
5. Data Processing:
    a. Open video in "Kinovea" software.
    b. Use Landing Error Scoring System[65] to grade landing for each trial.

Table C-13. Single Leg Hops Methods

1. **Equipment:**
    a. 6m long and 15 cm wide tape measure secured to floor.
    b. Stopwatch & Orthopaedic tape measure
2. **Singe-leg Hops:**
    a. Participant will perform at least 2x practice trials or until comfortable on each limb for each test.
    b. Participant must be in control and "stick" all landings for all hops except 6m timed. Failed trial if unable to maintain balance and foot position on landing limb.
    c. Participant must complete 3 successful trials on uninvolved limb, then 3 successful trials on involved limb.
    d. Record hop distance in cm, record hopping time in seconds.
    e. Single hop for distance: Participant performs 1 hops as far as possible, hopping and landing on the same limb.
    f. Triple hop for distance: Participant performs 3 consecutive hops as far as possible, hopping and landing on the same limb.
    g. Cross-over hop for distance: 3 consecutive hops for distance while crossing from left to right over the 15 cm line.
    h. 6-m times hop: Participant performs as many consecutive hops as far as necessary to travel 6m as fast as possible, hopping and landing on the same limb. Use stopwatch to record time
3. **Data Processing:**
    a. Calculate the average hopping distance/time for the three trials on each limb.
    b. Single limb: Normalize by leg length
    c. Limb symmetry: = (involved value/uninvolved value)*100

Table C-14. Sample Size Estimation

We estimate we will need 18 participants per group, 72 total participants, for statistical power ($\beta = 0.80$, $\alpha = 0.05$). We determined our sample size estimate based on effects sizes and variances from previous studies that used similar outcomes, methodology, and patient populations as the current study. We determined using an expected large effect size of $d = 0.95$ would sufficient for each of our primary variables based off previous studies.

Quadriceps Avoidance Studies
Hart 2010: d = 0.94
Average ES = 0.94

Quadriceps Force Control Studies
Smith et al. 2014: d = 1.02 [0.17, 1.87], St. dev. = 1.18
Smith et al. 2014: d = 1.54 [0.62, 2.54], St. dev. = 1.04
Average ES = 1.28

Gamma-loop Studies
Konishi et al. 2002: d = 1.29 [0.37, 2.21], St. dev. = 6.65
Konishi et al. 2011: d = 2.78 [1.52, 4.05], St. dev. = 5.10
Average ES = 2.04

APPENDIX D
Additional Results

Figure D-1. Means and 90% Confidence Intervals of Inter-Limb Vertical Ground Reaction Forces during Walking in Early, Mid, Late ACLR and Control Groups

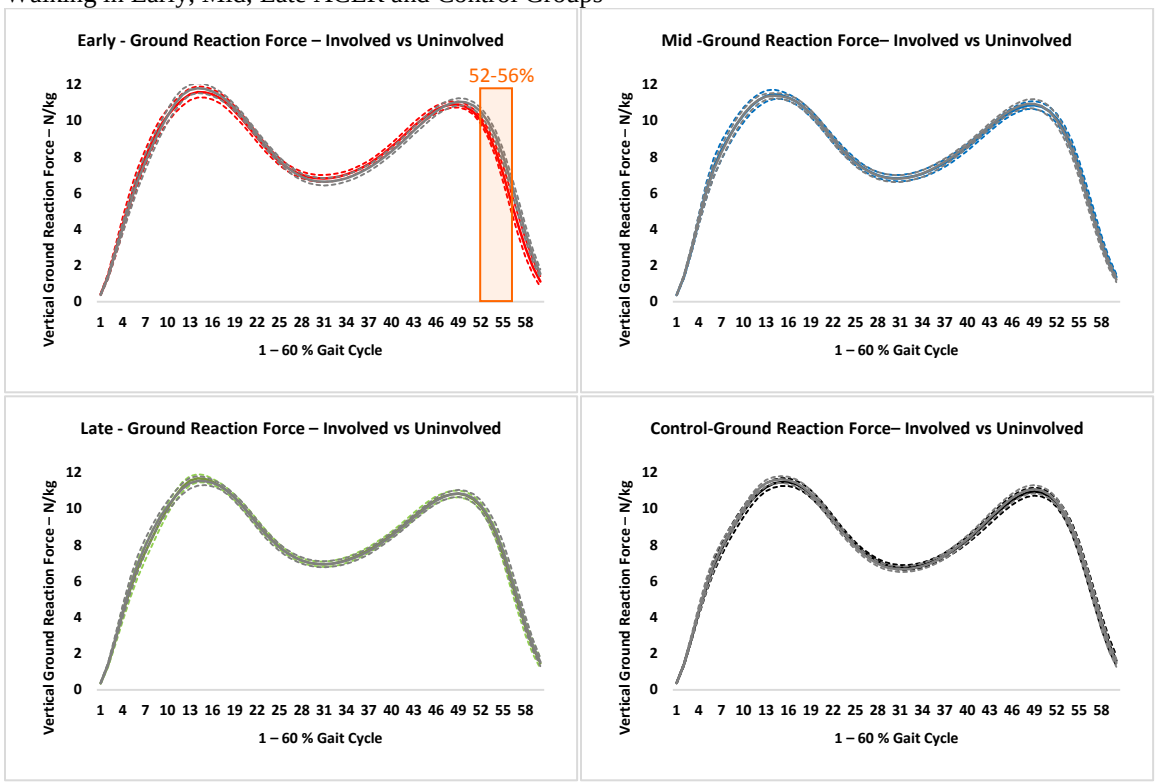


Figure D-2. Means and 90% Confidence Intervals of Inter-Limb Knee Sagittal Kinematics during Walking in Early, Mid, Late ACLR and Control Groups

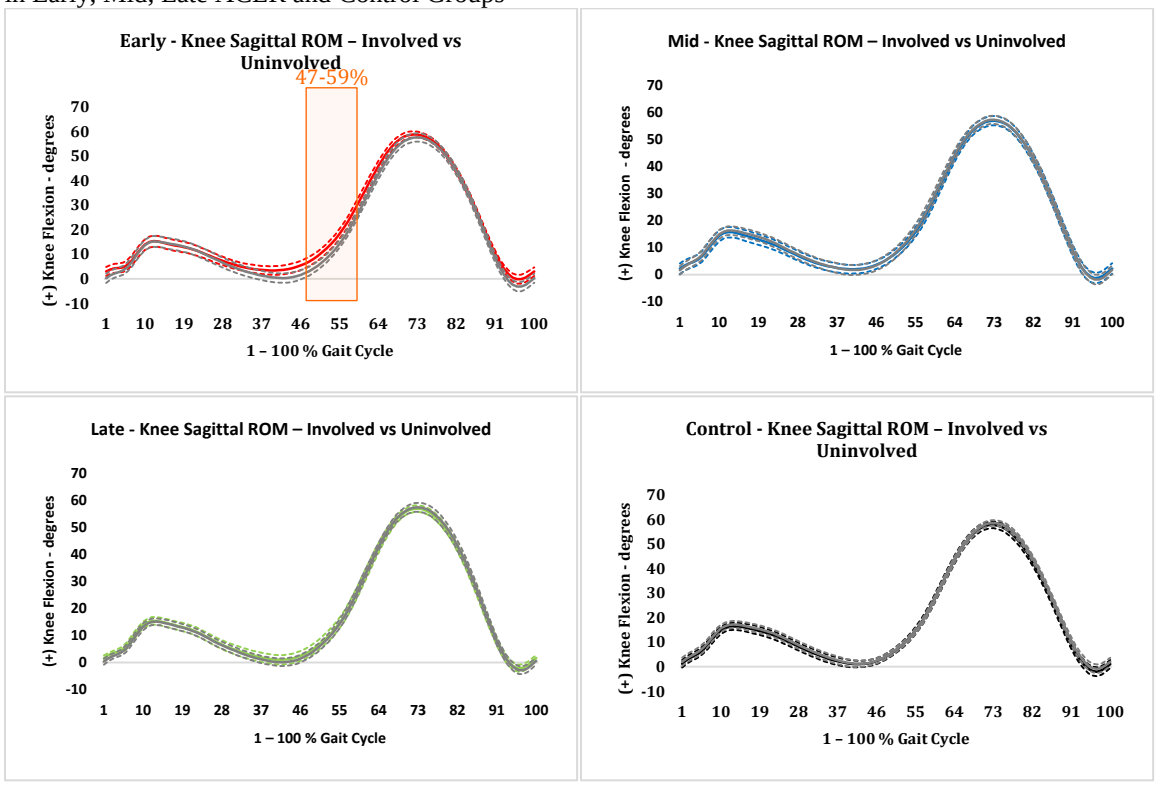


Figure D-3. Means and 90% Confidence Intervals of Inter-Limb Knee Sagittal Kinetics during Walking in Early, Mid, Late ACLR and Control Groups

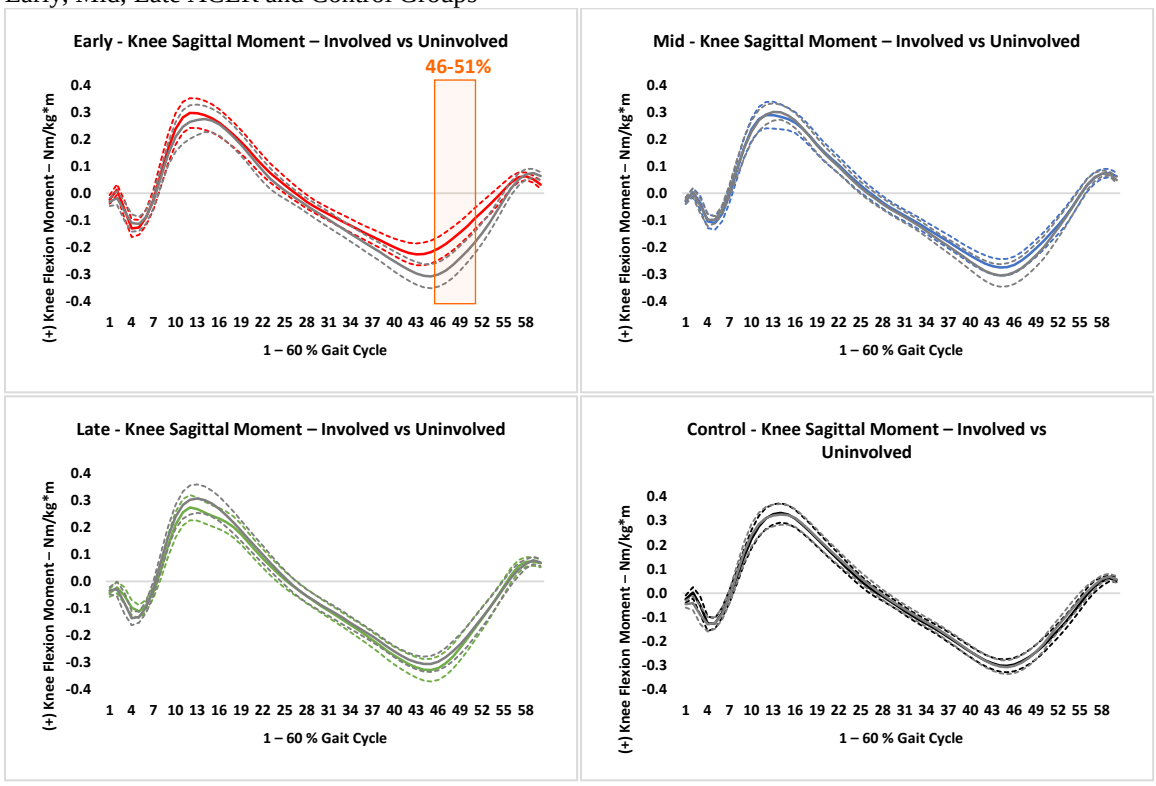


Figure D-4. Means and 90% Confidence Intervals of Inter-Limb Hip Sagittal Kinematics during Walking in Early, Mid, Late ACLR and Control Groups

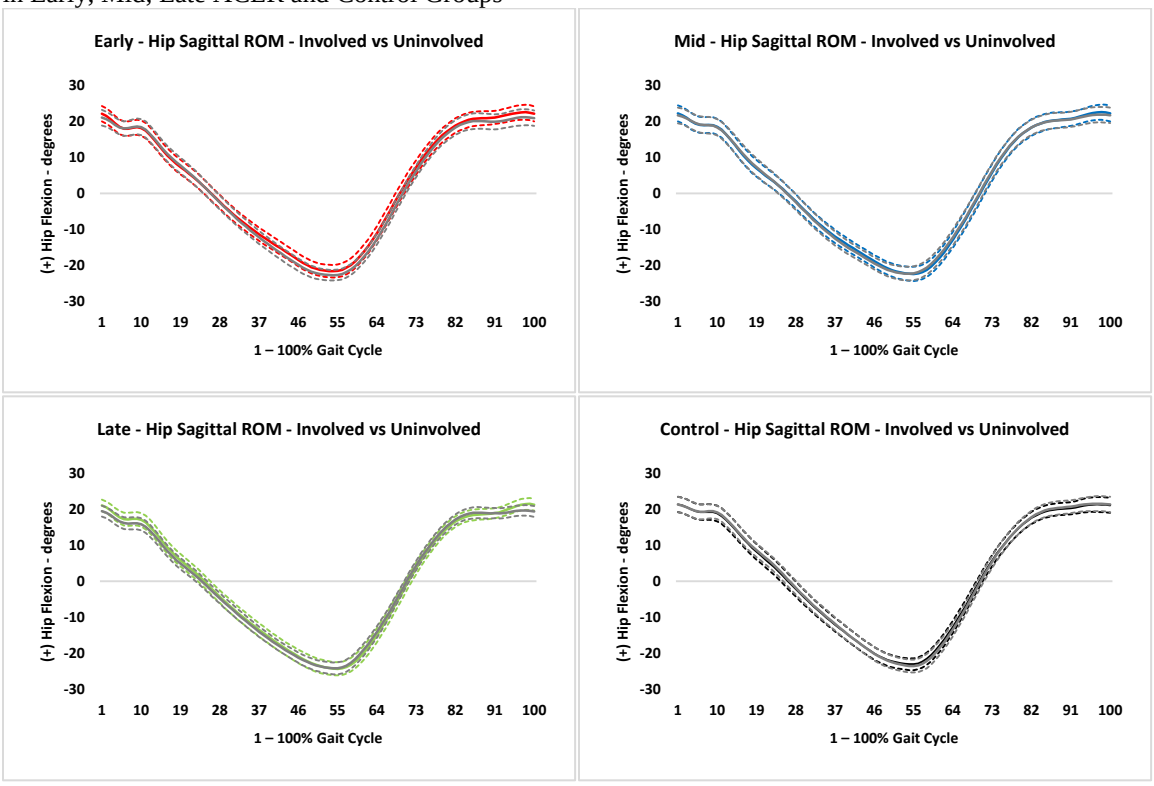


Figure D-5. Means and 90% Confidence Intervals of Inter-Limb Hip Sagittal Kinetics during Walking in Early, Mid, Late ACLR and Control Groups

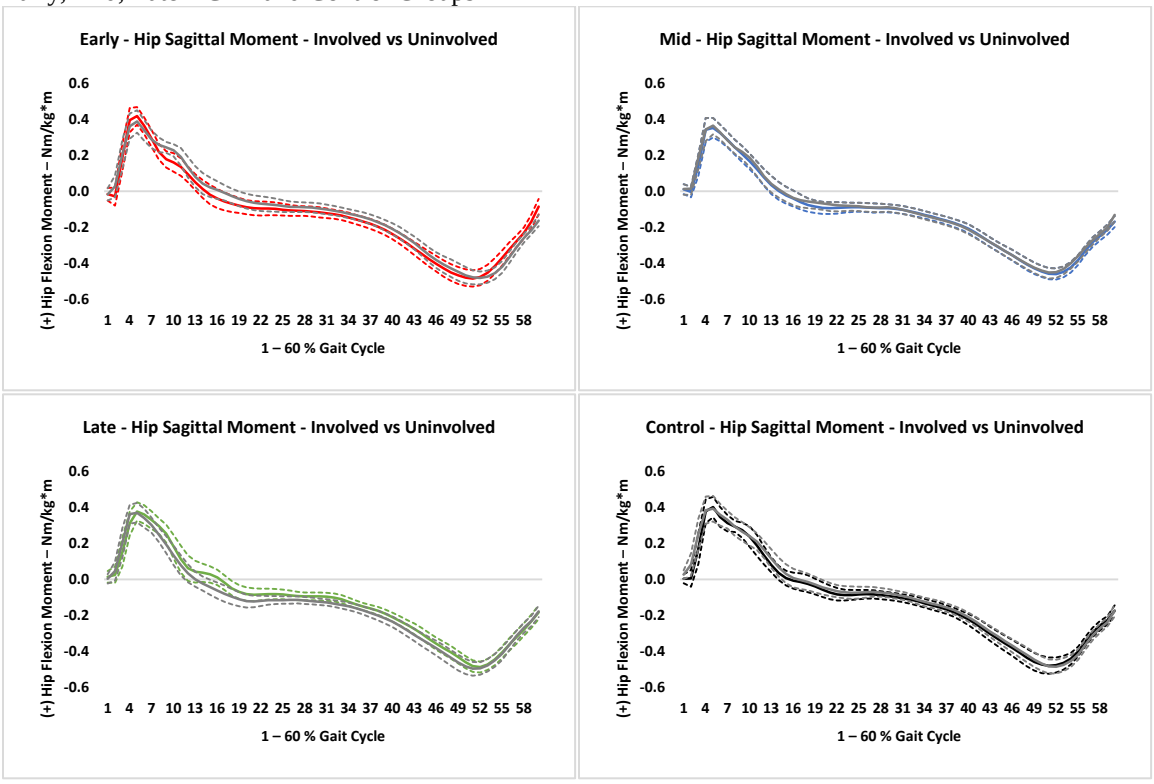


Figure D-6. Means and 90% Confidence Intervals of Inter-Limb Knee Frontal Kinematics during Walking in Early, Mid, Late ACLR and Control Groups

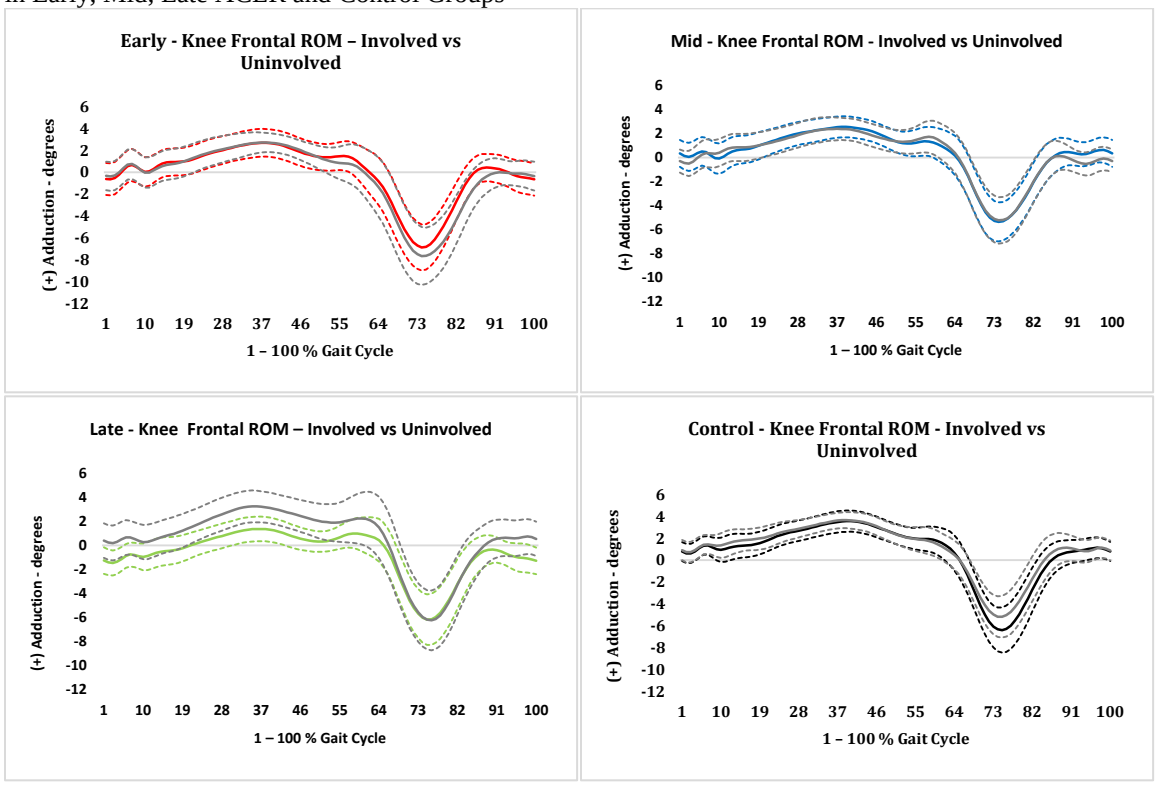


Figure D-7. Means and 90% Confidence Intervals of Inter-Limb Knee Frontal Kinetics during Walking in Early, Mid, Late ACLR and Control Groups

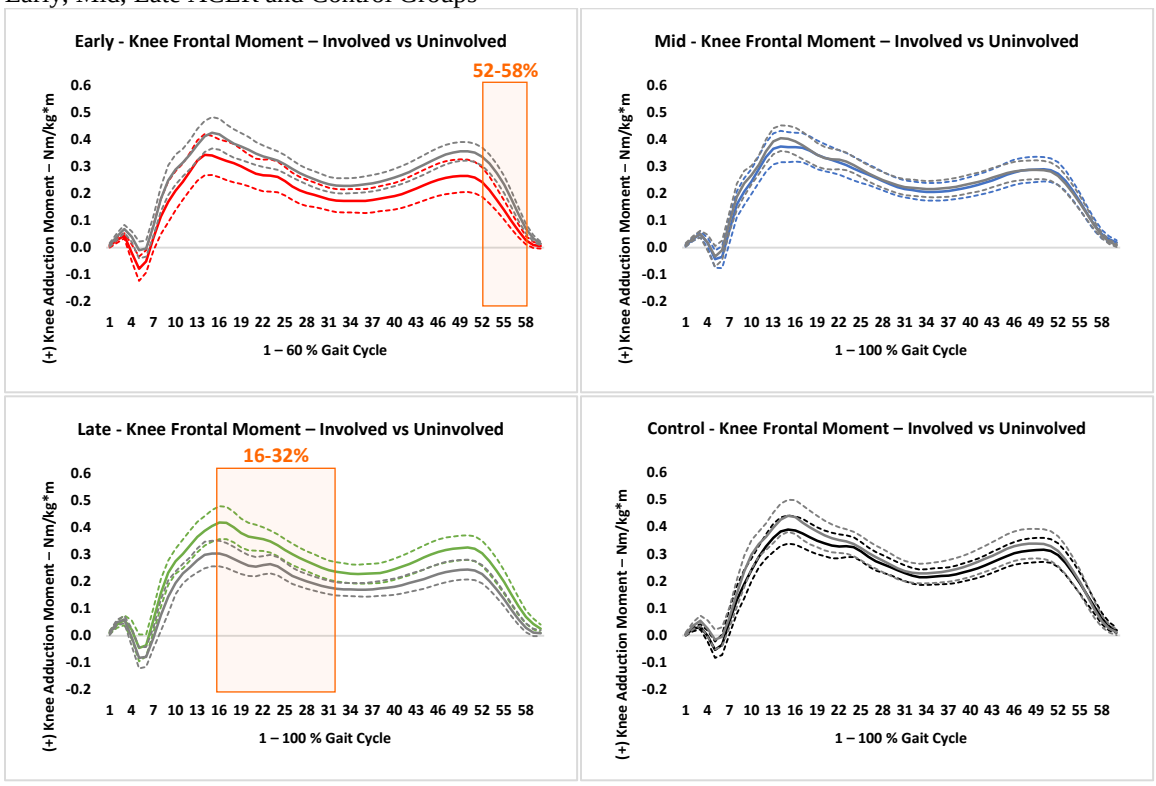


Figure D-8. Means and 90% Confidence Intervals of Inter-Limb Hip Frontal Kinematics during Walking in Early, Mid, Late ACLR and Control Groups

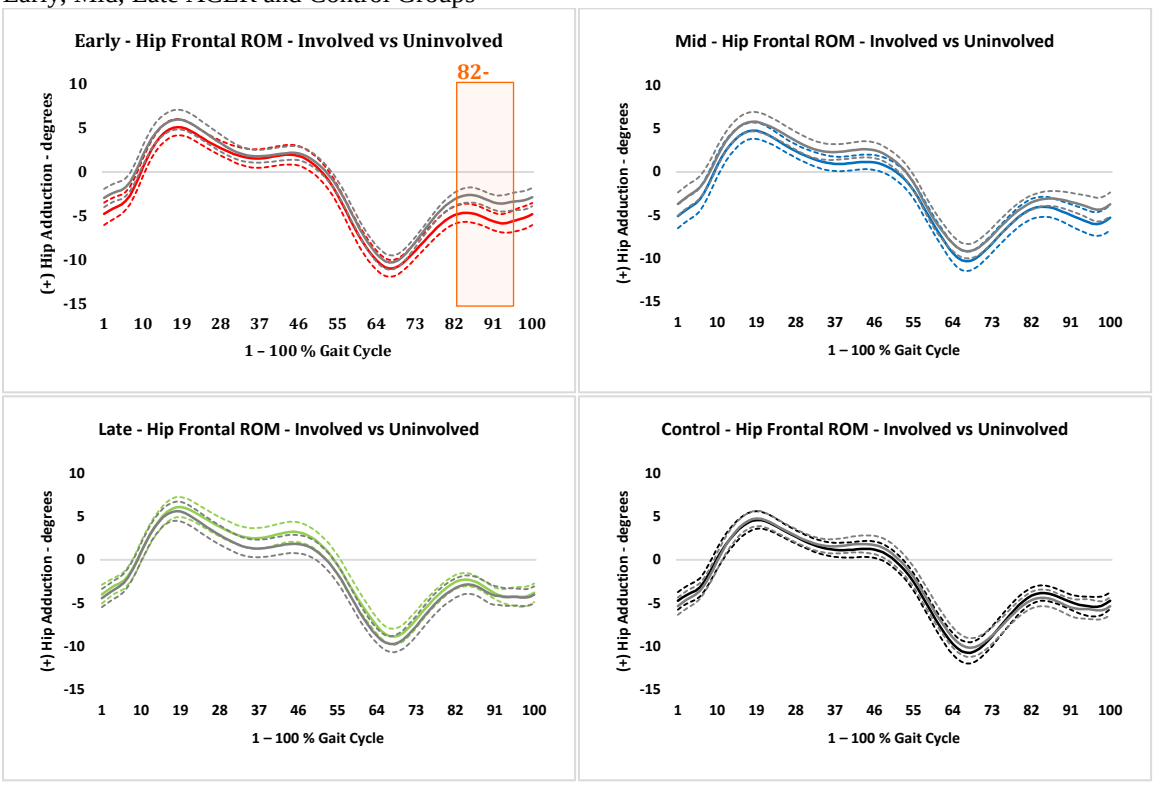


Figure D-9. Means and 90% Confidence Intervals of Inter-Limb Hip Frontal Kinetics during Walking in Early, Mid, Late ACLR and Control Groups

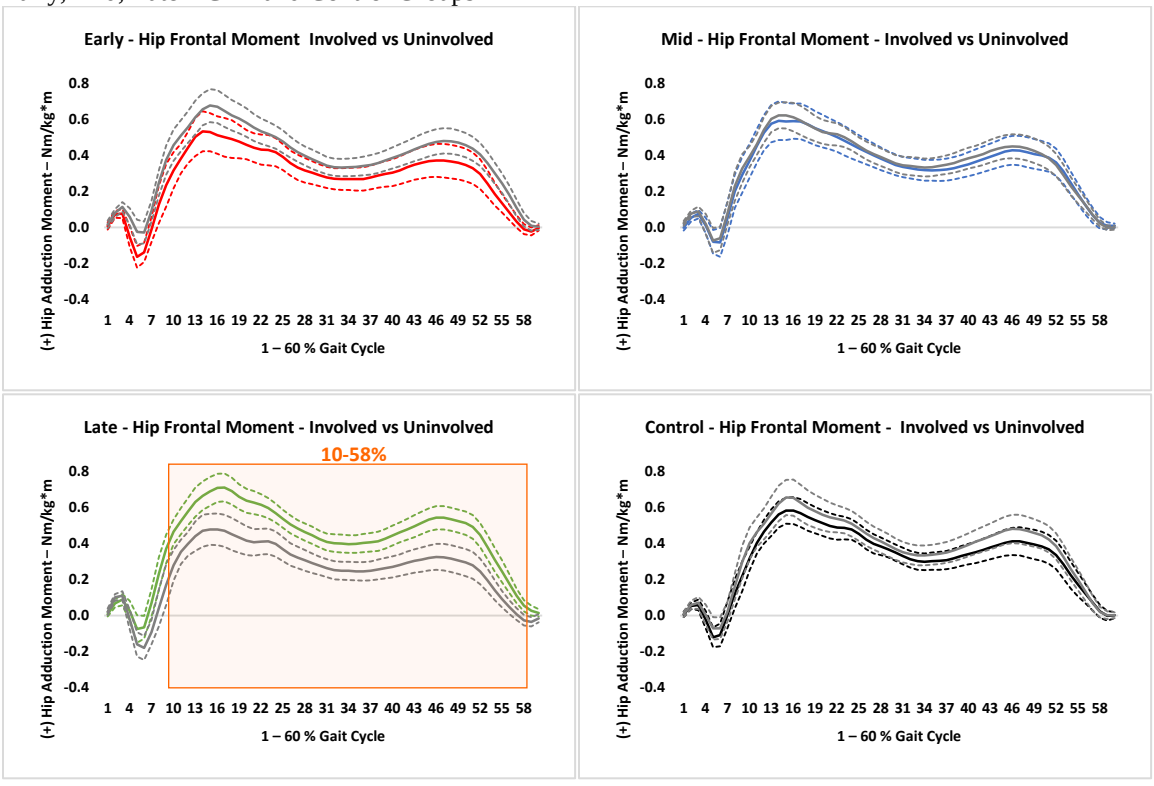


Figure D-10. Means and 90% Confidence Intervals of Inter-Limb Vertical Ground Reaction Force during Jogging in Early, Mid, Late ACLR and Control Groups

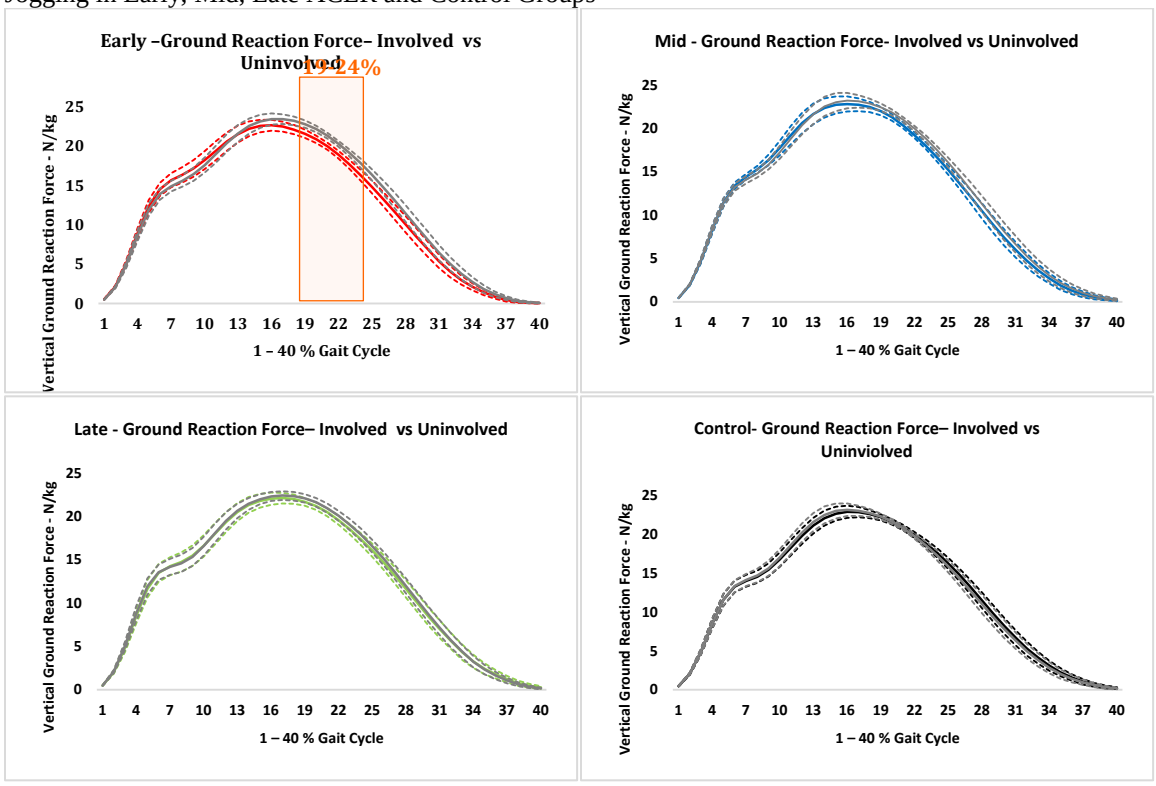


Figure D-11. Means and 90% Confidence Intervals of Inter-Limb Knee Sagittal Kinematics during Jogging in Early, Mid, Late ACLR and Control Groups

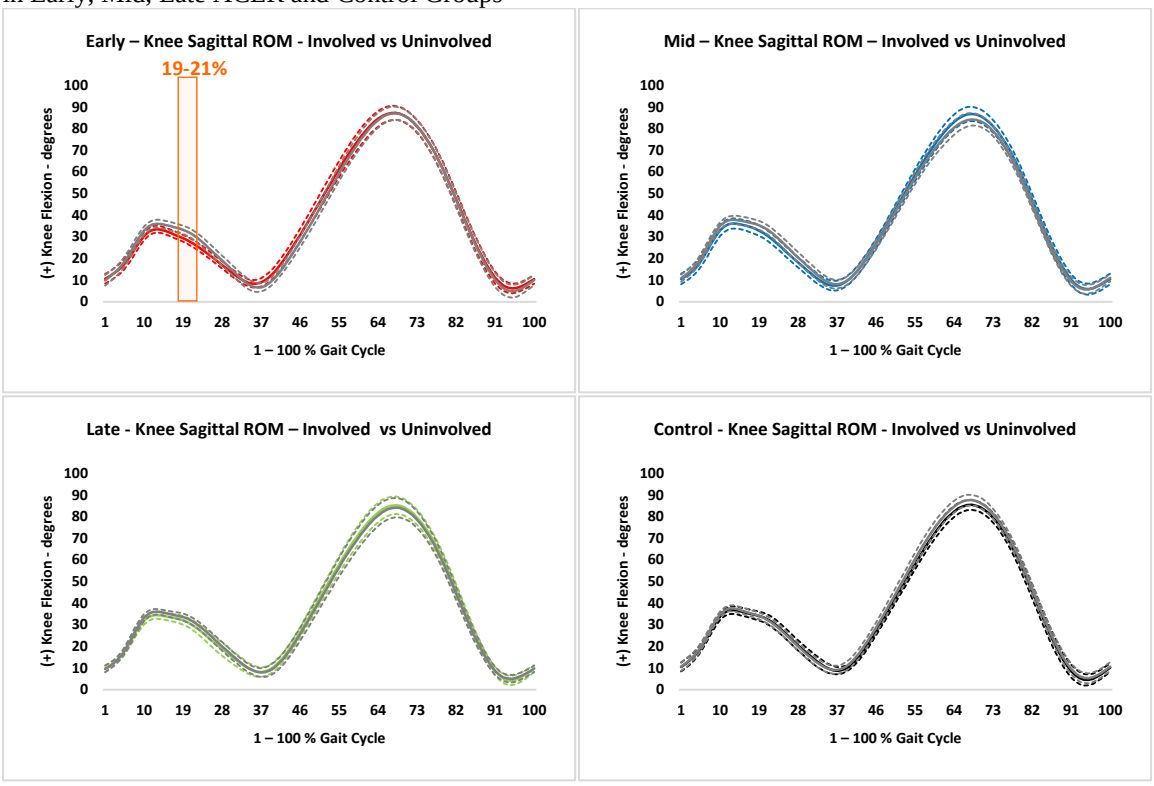


Figure D-12. Means and 90% Confidence Intervals of Inter-Limb Knee Sagittal Kinetics during Jogging in Early, Mid, Late ACLR and Control Groups

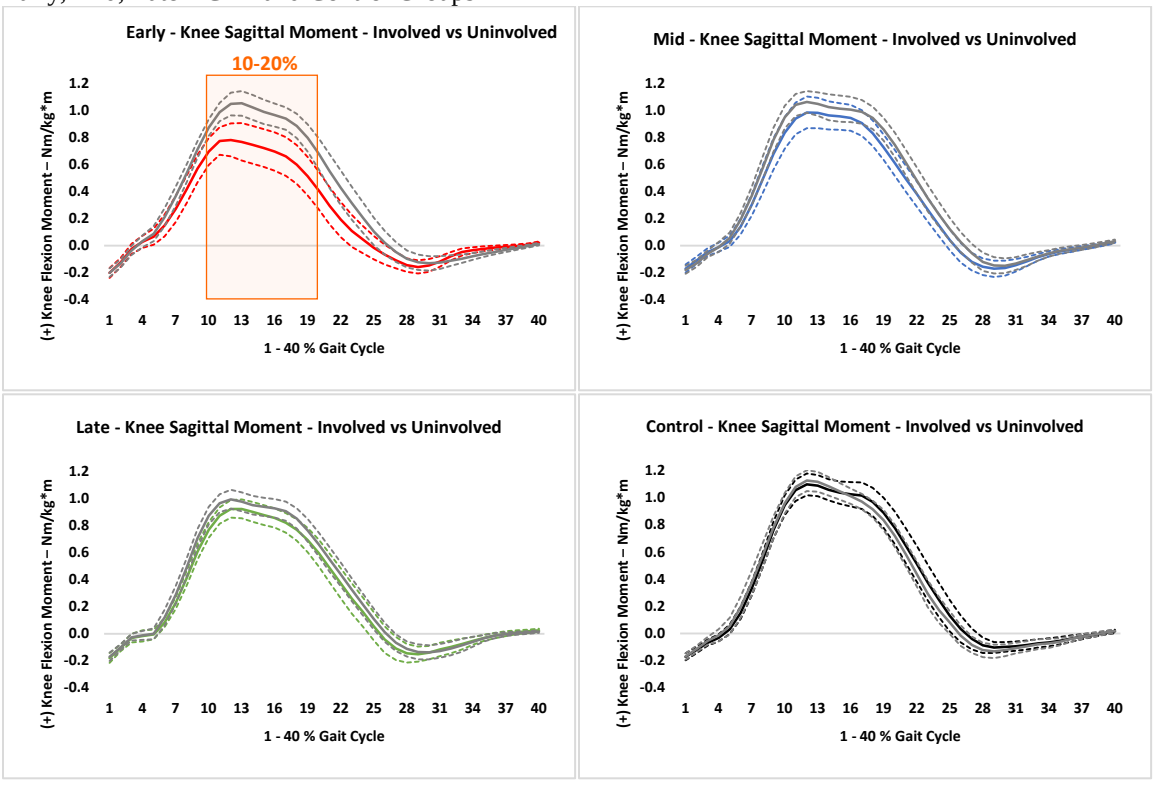


Figure D-13. Means and 90% Confidence Intervals of Inter-Limb Hip Sagittal Kinematics during Jogging in Early, Mid, Late ACLR and Control Groups

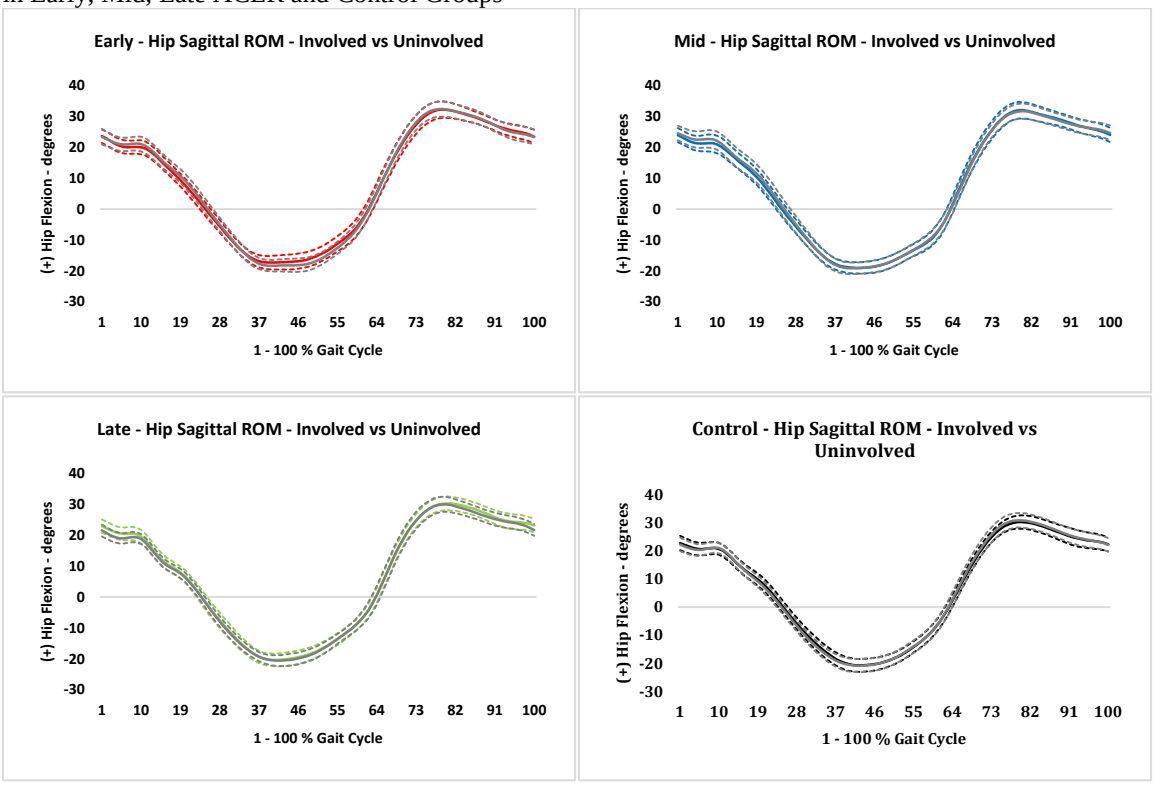


Figure D-14. Means and 90% Confidence Intervals of Inter-Limb Hip Sagittal Kinetics during Jogging in Early, Mid, Late ACLR and Control Groups

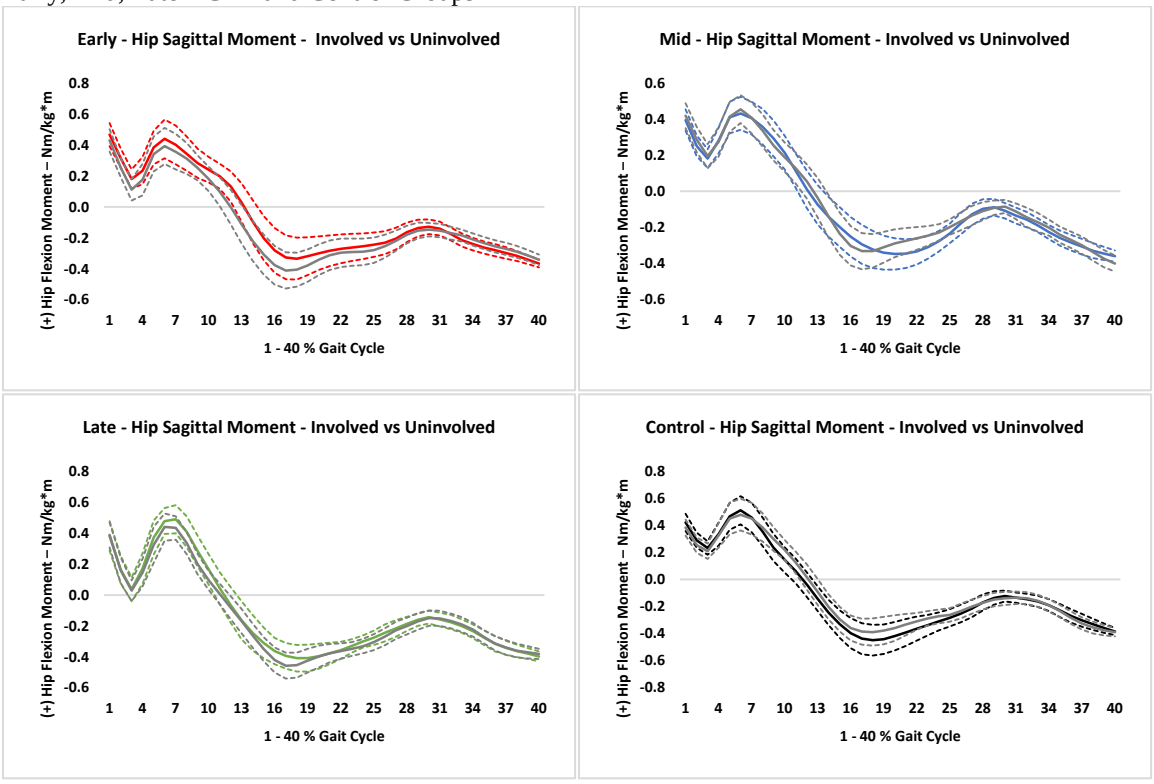


Figure D-15. Means and 90% Confidence Intervals of Inter-Limb Knee Frontal Kinematics during Jogging in Early, Mid, Late ACLR and Control Groups

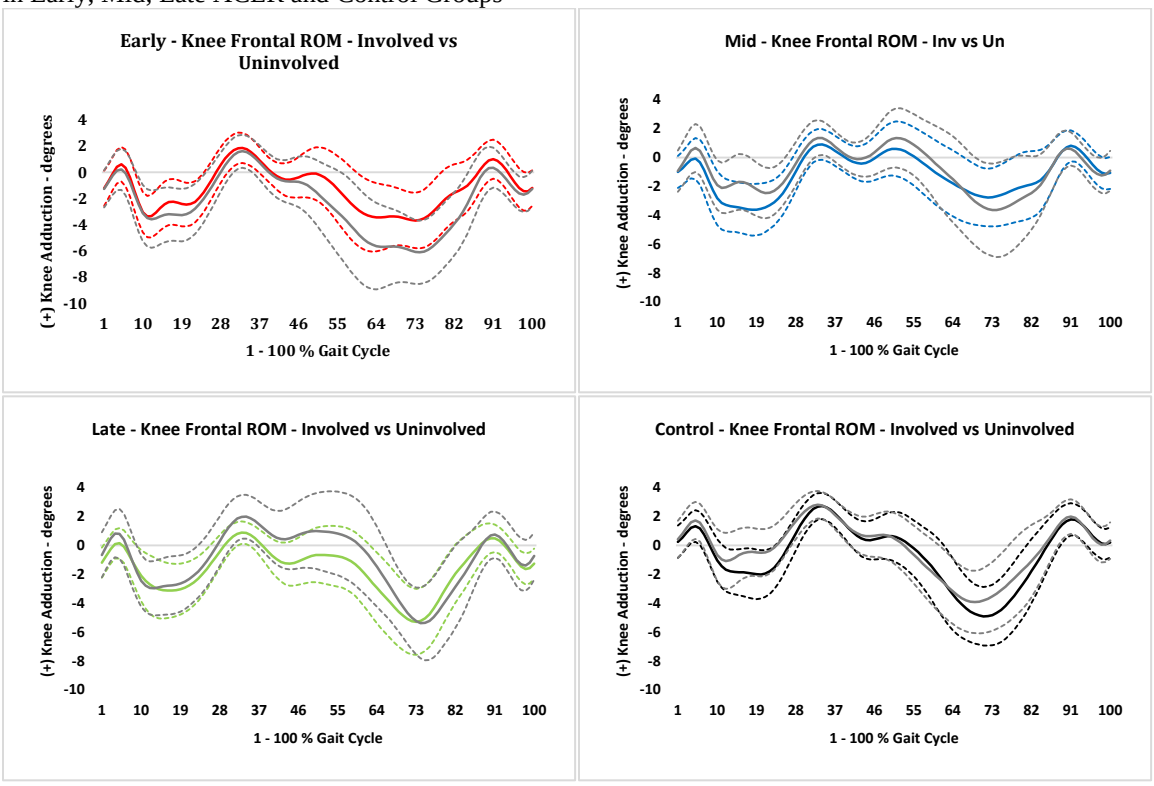


Figure D-16. Means and 90% Confidence Intervals of Inter-Limb Knee Frontal Kinetics during Jogging in Early, Mid, Late ACLR and Control Groups

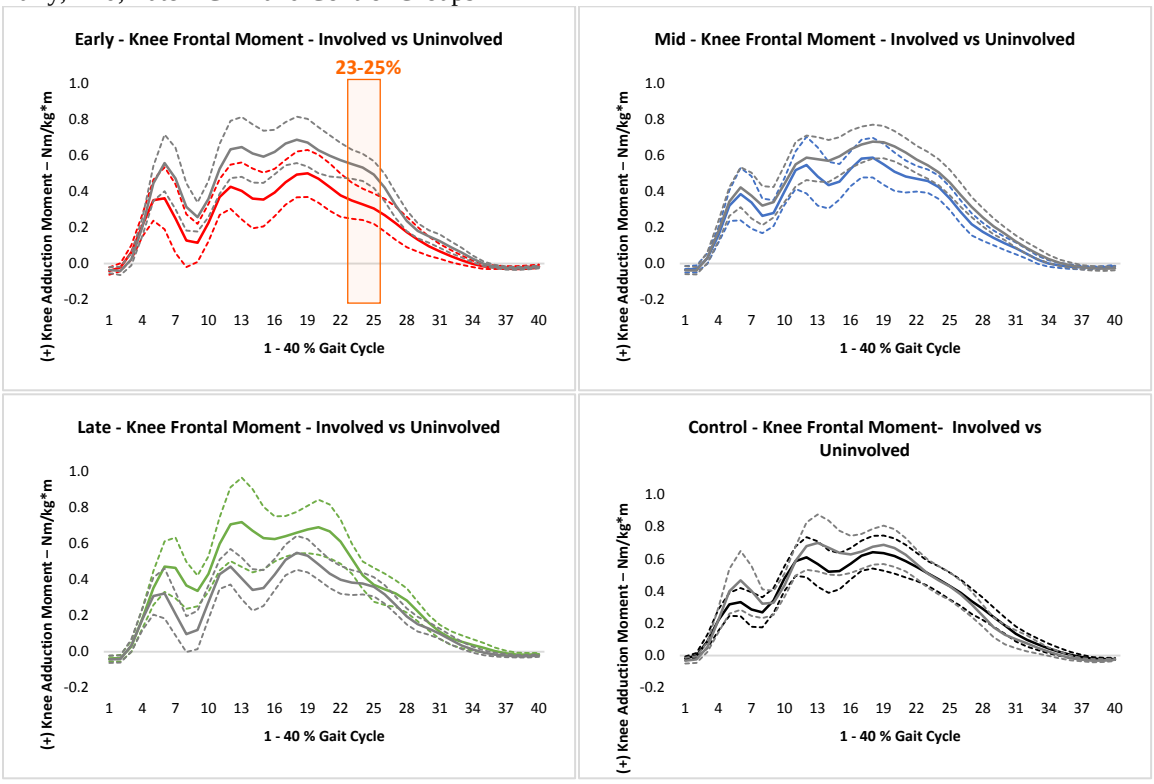


Figure D-17. Means and 90% Confidence Intervals of Inter-Limb Hip Frontal Kinematics during Jogging in Early, Mid, Late ACLR and Control Groups

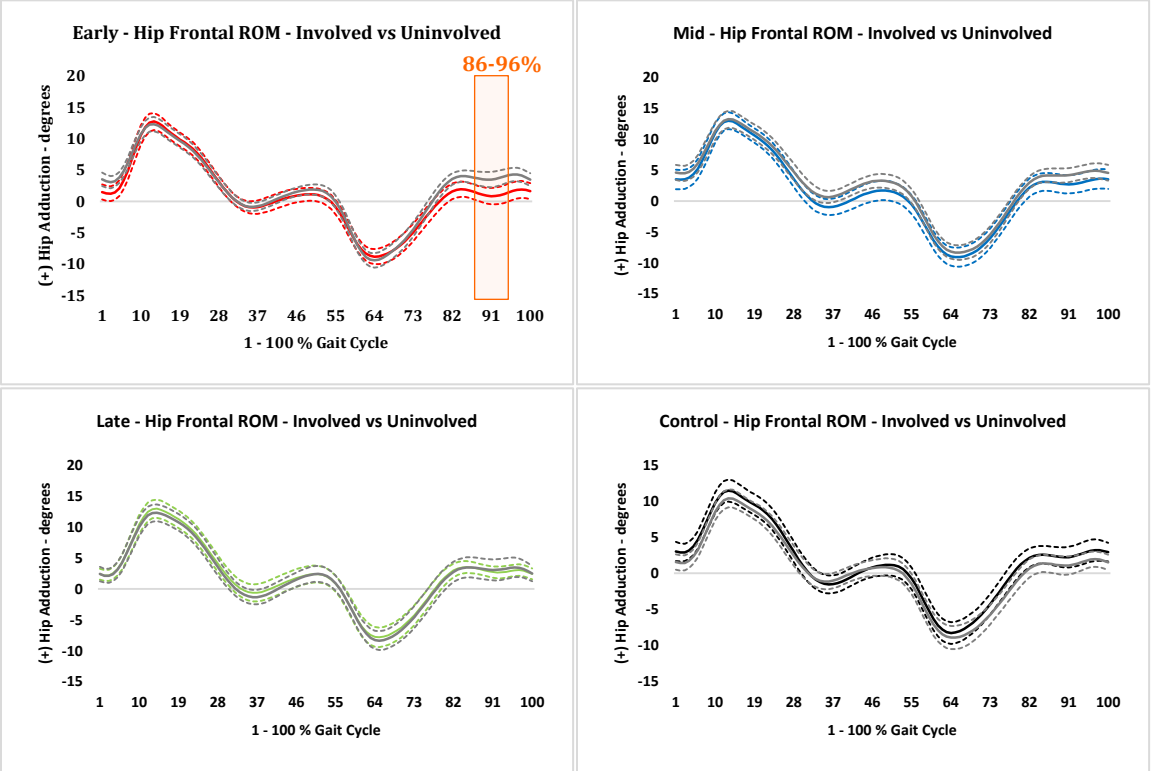


Figure D-18. Means and 90% Confidence Intervals of Inter-Limb Hip Frontal Kinetics during Jogging in Early, Mid, Late ACLR and Control Groups

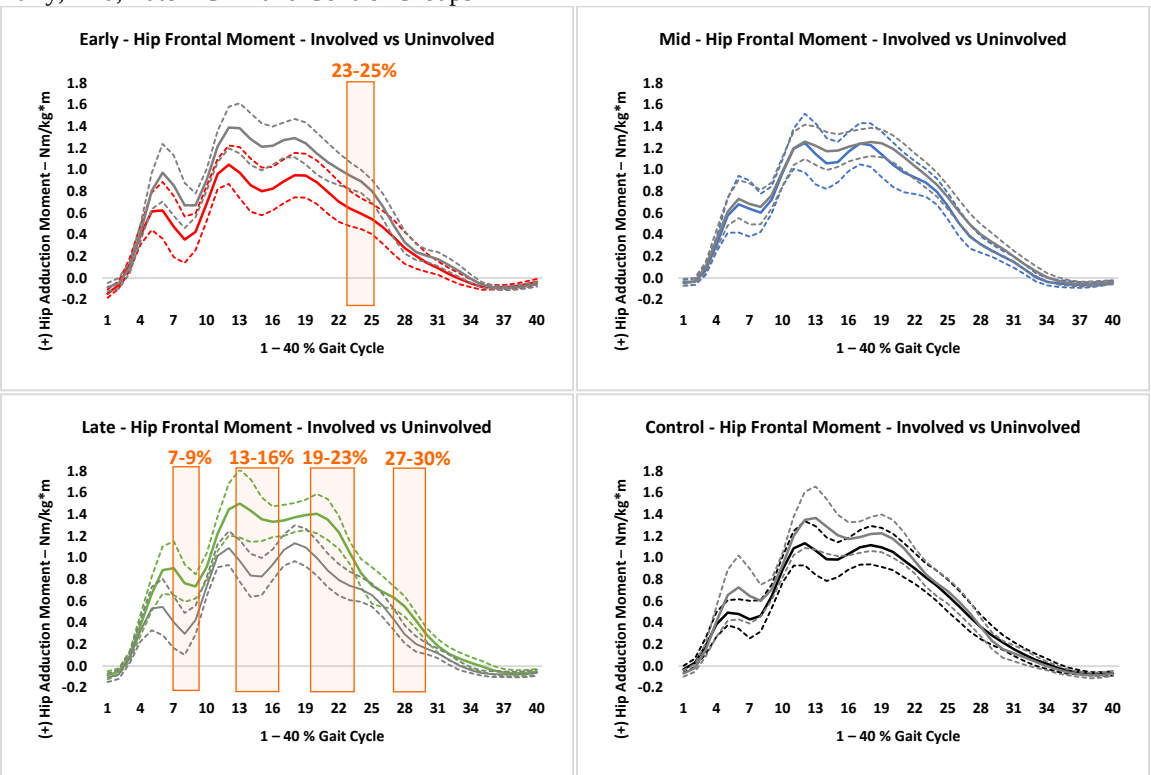


Table D-1. Manuscript II Demographics in Early, Mid, Late and Control Groups

	Early ACLR (n = 19)	Mid ACLR (n = 20)	Late ACLR (n = 18)	Control (n = 20)
Sex $_{F,M}$	12 F, 7 M	16 F, 4 M	12 F, 6 M	13 F, 7 M
Age $_{years}$	21.6 ± 4.0	20.5 ± 2.2	26.7 ± 44 [a]	22.4 ± 3.2
Mass $_{kg}$	68.5 ± 15.2	68.5 ± 9.9	69.5 ± 12.7	68.9 ± 13.1
Height $_{m}$	1.71 ± .12	1.73 ± .09	1.73 ± .10	1.71 ± .13
KOOS $_{0\text{-}100}$	88.8 ± 6.9 [b]	90.7 ± 5.5 [b]	92.1 ± 7.2 [b]	99.3 ± 1.8
Godin	69.9 ± 22.4	74.5 ± 13.0	59.9 ± 26.4	70.5 ± 17.9
Post-Op Time, $_{months}$	17 ± 6 [c]	39 ± 8 [c]	103 ± 33 [c]	NA
Graft-Type	BTB 7, HS 11, Cad 1	BTB 11, HS 5, Cad 4	BTB 10, HS 5, Cad 3	NA

[a] Significantly greater than all other groups (P<.001)
[b] Significantly lower than control group (P<.001)
[c] Significantly different from other ACLR groups

Figure D-19: Isometric Force Standard Deviation (SD), Coefficient of Variation (CV), and Root Mean Square Error (RMSE) in Early, Mid, Late ACLR & Controls

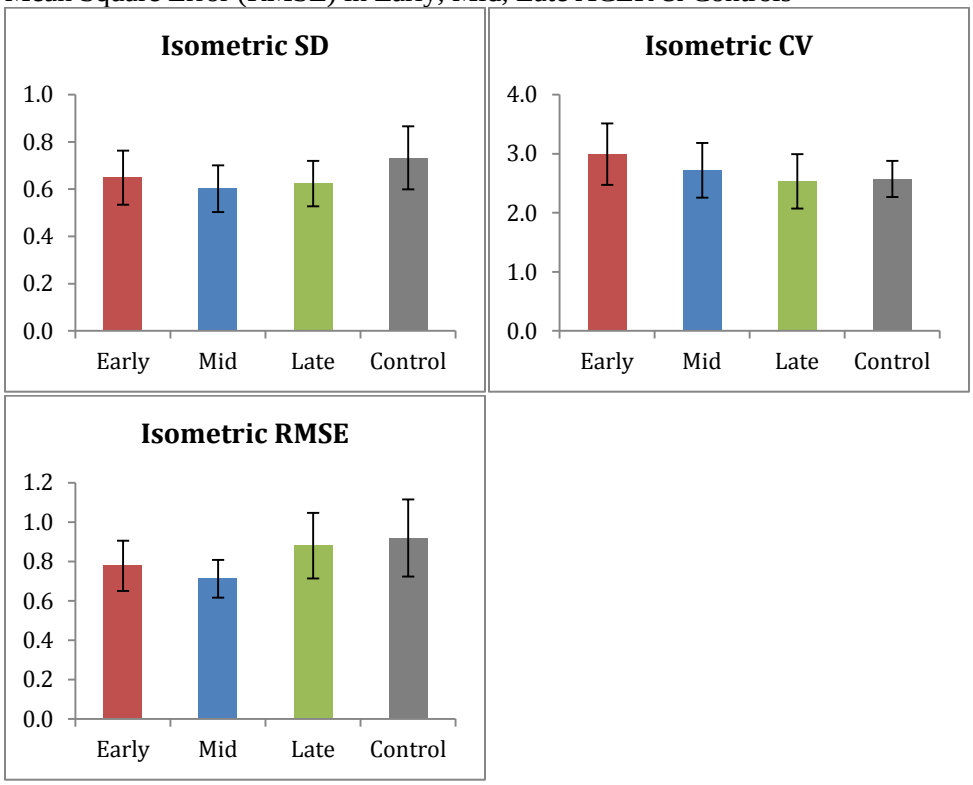


Figure D-20: Concentric Force Standard Deviation (SD), Coefficient of Variation (CV), and Root Mean Square Error (RMSE) in Early, Mid, Late ACLR & Controls

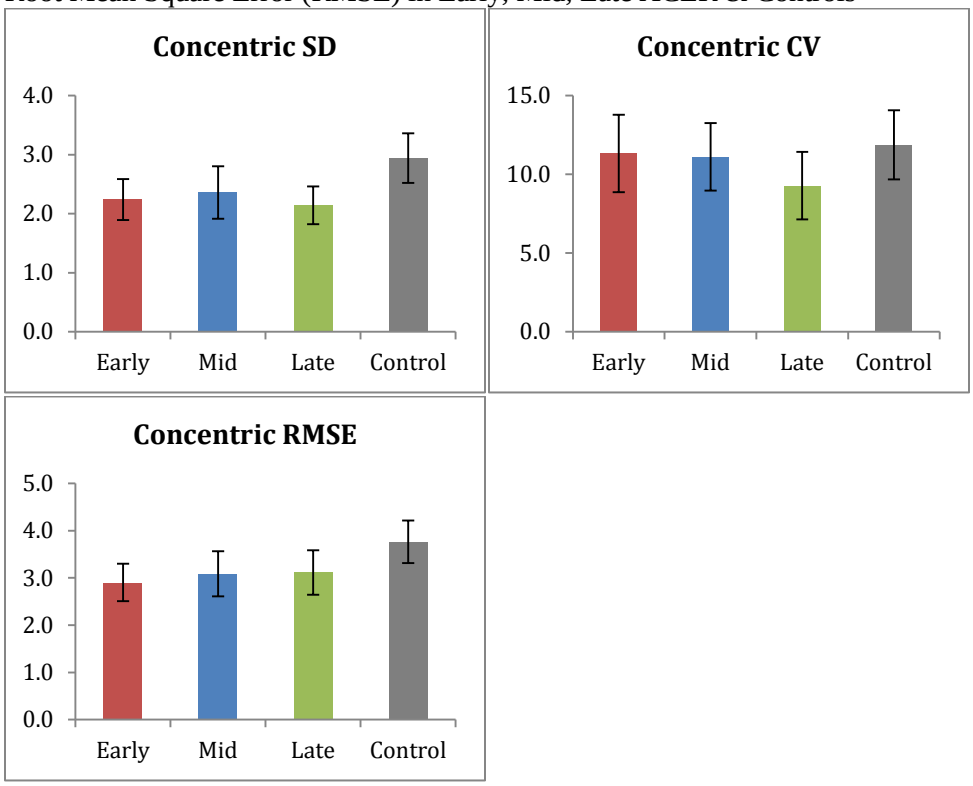


Figure D-21: Eccentric Force Standard Deviation (SD), Coefficient of Variation (CV), and Root Mean Square Error (RMSE) in Early, Mid, Late ACLR & Controls

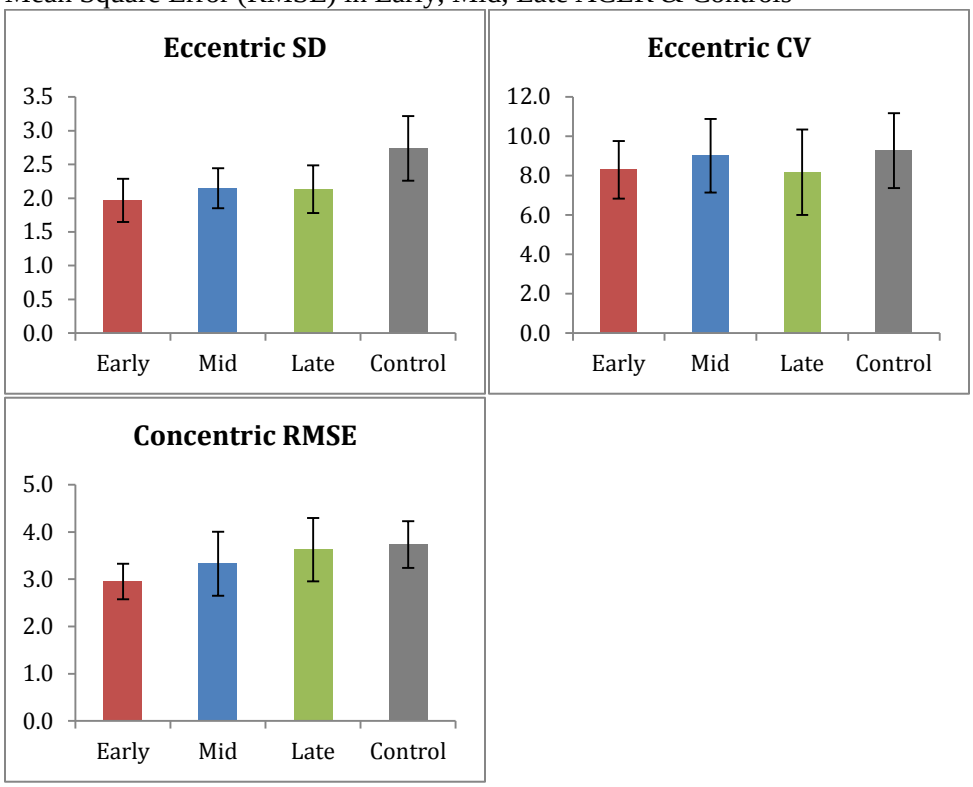


Table D-2. Manuscript III Demographics in Early, Mid, Late and Control Groups

	Early ACLR (n = 16)	Mid ACLR (n = 20)	Late ACLR (n = 14)	Control (n = 18)
Sex	10F, 6 M	16 F, 3 M	11 F, 5 M	12 F, 7 M
Age	21.2 ± 4.1	20.6 ± 2.2	28.1 ± 3.9	22.3 ± 3.3
Mass	66.6 ± 11.1	67.6 ± 9.7	70.8 ± 13.9	69.1 ± 13.4
Height	1.70 ± .09	1.72 ± .09	1.73 ± .10	1.71 ± .13
KOOS	87.9 ± 7.1	91.6 ± 5.5	91.4 ± 7.9	99.2 ± 1.9
Godin	66.4 ± 21.6	74.5 ± 13.0	58.4 ± 29.2	70.2 ± 18.7
Post-Op	16.9 ± 5.9	41.1 ± 8.4	111.6 ± 31.6	NA

Figure D-22: Baseline and Post-vibration Quadriceps MVIC in Early, Mid, Late ACLR and Control groups

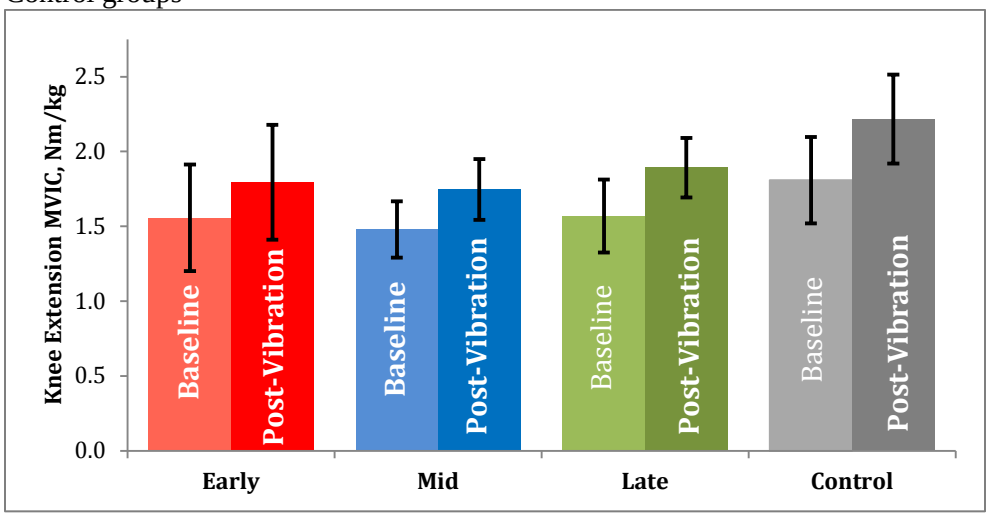
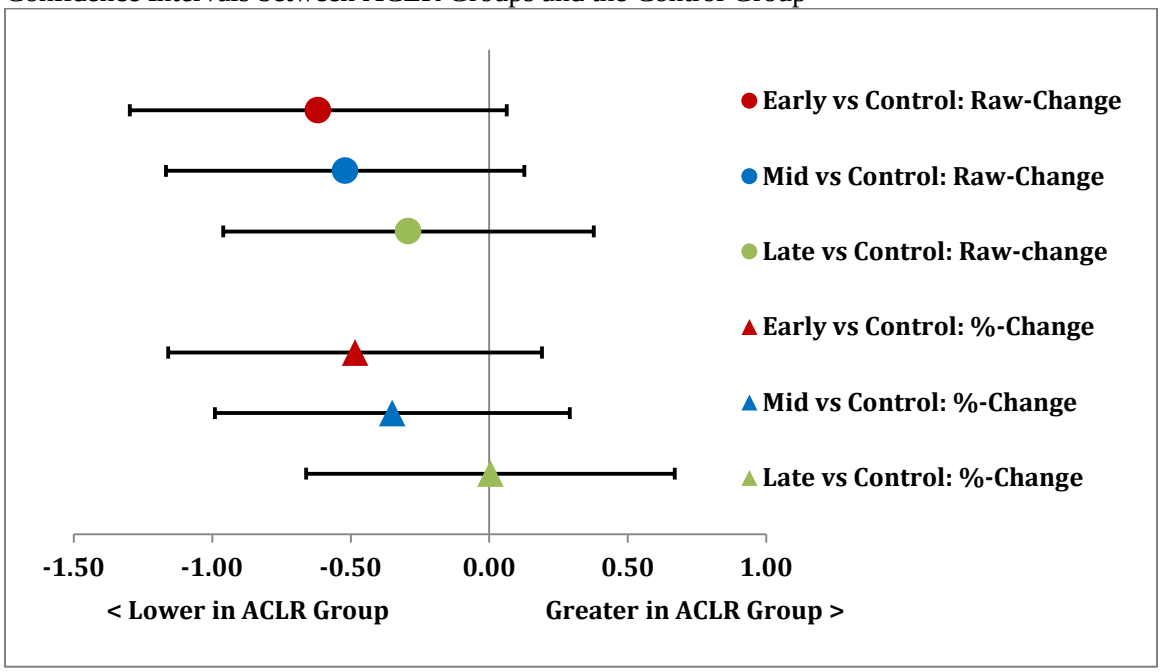


Figure D-23: Raw-Change and Percent Change in MVIC after Vibration Effect-Sizes and 95% Confidence Intervals between ACLR Groups and the Control Group



APPENDIX E

Recommendations for Future Research

- Are adaptations in trunk kinematics associated with adaptations in frontal plane knee kinetics in patients with a history ACLR, and are trunk kinematics during gait different in ACLR patients at sequential time-frames post-surgery?
- Are adaptations in trunk motion associated with adaptations in spatiotemporal measures of stance width, length, and time in patients with a history ACL reconstruction, and are these variables different in ACLR patients at sequential time-frames post-surgery
- Is hip abductor weakness a factor contributing to increased knee adduction moments in patients with a history of ACL reconstruction?
- Is submaximal and maximal muscle function associated with the distribution of type I and type II quadriceps muscle fibers in ACLR knees?
- What target force intensity and contraction mode is optimal for evaluating submaximal muscle function in ACLR knees?
- Can patellar tendon vibration be utilized in combination with therapeutic exercises to improve quadriceps muscle function faster and better than exercise alone?
- Can we achieve a similar magnitude increase in quadriceps strength following a shorter, more clinically feasible, vibration treatment?
- What are the optimum vibration amplitudes for studying and treating quadriceps muscle weakness in ACLR knees?
- What factors contribute to whether an ACLR knee experiences a small or large magnitude increase in quadriceps strength following patellar tendon vibration

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