The Association Between Quadriceps Activity and Loading Variables During Walking Gait in Individuals with ACL-R

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April 18, 2016

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Chapter 1: Introduction

The anterior cruciate ligament (ACL) is the most frequently disrupted knee ligament, injured at the highest incidence among physically active individuals under the age of 30.[1] Surgical reconstruction of the ACL aims to increase knee stability, reduce the chance of further injury, and facilitate the return to normal activities and sports. However, ACL reconstruction (ACL-R) does not restore the knee to its pre-injury state,[2] and is associated with a substantial increase in the risk of early onset knee osteoarthritis (OA).[3-8] Among a cohort of 122 male soccer players with ACL-R, von Porat et al.[8] found that 95 (78%) showed radiographic signs of knee OA 14 years after the initial injury. Culvenor et al.[9] reported considerable joint disease in one-third of individuals within one year following ACL-R. Similarly, recent findings suggest cartilage changes indicative of OA during the first two years after ACL injury.[10] In young adults, joint injury is the most common risk factor for OA and can lead to its development prior to patients reaching 50 years of age.[11] Approximately 12% of symptomatic OA of the hip, knee, and ankle arises from joint injury and is thus characterized as post-traumatic osteoarthritis (PTOA).[12] PTOA affects 5.6 million individuals in the United States and creates a financial burden of more than $3 billion in direct healthcare costs.[11] With incidences of ACL-R historically rising,[13] identifying factors that contribute to knee OA development that can be targeted via intervention is critical.

Knee OA progression is provoked by biomechanical forces that cause structural joint deterioration.[14] Ground reaction forces are the primary external contributors to knee joint loading during human movement and can reach magnitudes up to three times body weight.[15,16] During gait, muscles and trabecular bone have been assumed to counteract most of the external forces at the knee joint, while other connective tissues such as articular cartilage and ligament account for

a small fraction of the loading.[17] Healthy articular cartilage provides a low-friction surface at the articulating surfaces of bones to allow for free movement of diarthrodial joints, while also distributing loads to minimize bony stress.[18] Eccentric quadriceps activity is the primary mechanism of force attenuation at the knee joint. Thus, when the quadriceps are impaired, more force attenuation is required from the other connective tissues. Chronic quadriceps dysfunction following ACL injury has been well documented[19,20] and can persist for several years, potentially impeding the ability to absorb impact loading and contributing to the development of knee OA.[21,22]

Quadriceps dysfunction has been associated with impulsive, or high rate, loading.[22,23] Impulsive loading produces microfractures in the trabecular and subchondral bone, subsequently increasing bone stiffness during remodeling.[24] The increase in bone stiffness decreases force attenuation capacity, facilitating cartilage break down and joint degeneration.[24] Mikesky et al.[25] reported that healthy women with weaker quadriceps displayed greater loading rates during gait. Appropriate quadriceps activation prior to heel strike (HS) is critical for attenuation of impact loading,[17] as it is essential for decelerating the limb. Diminished quadriceps activity is thus characteristic of impulsive loading.[23,25] Multiple studies support the notion that diminished quadriceps function leads to impulsive loading during gait,[23,26-28] which potentially contributes to OA development and progression. There is further evidence to suggest the existence of an independent relationship between rate of loading and joint degeneration, regardless of the peak magnitude of the load.[26]

Near the end of the swing phase, muscles control the lower limb in preparation for ground contact. In order to decelerate the lower limb prior to HS, the quadriceps are normally active during the terminal swing phase. Earlier onset of quadriceps activity prior to HS has been

associated with lesser loading rates.[22,23] Healthy individuals exhibiting impulsive loading have delayed muscular activation compared to those with normal gait patterns, and rely on firm contact with the ground to decelerate the limb rather than muscle activity.[22] While timing of this activation is key, there also must be significant activation amplitude of the quadriceps to effectively slow the lower limb during its decent towards HS. Quadriceps activation deficits following ACL-R likely contribute to knee OA development, as the alterations of muscle forces affect natural loading conditions during locomotion.[21,29,30] Lower activity of the vastus medialis and rectus femoris prior to HS is linked to impulsive loading in individuals with radiographic, but asymptomatic, knee OA.[17] Furthermore, individuals with quadriceps weakness resulting from ACL-R tend to adopt quadriceps avoidance gait patterns.[21] Palmieri-Smith et al.[31] showed that lower preparatory activity of the quadriceps resulted in greater loading at the knee by increasing peak GRF, decreasing knee flexion angles, and decreasing knee extension moments. Thus, altered quadriceps activation timing and amplitude may contribute to impulsive loading that could lead to joint degeneration following ACL-R.

Quadriceps dysfunction following ACL-R may contribute to the development of OA due to the inability of the muscles to attenuate impact forces. Both the timing and amplitude of quadriceps activity early in the gait cycle appear to be important factors in decreasing loading rates. Because gait is a repetitive and perpetual task, slight changes in loading rates may have substantial effects on the articular cartilage of the knee joint. However, the influence of quadriceps activation characteristics on impulsive loading during gait has yet to be evaluated in individuals with ACL-R. Therefore, the purpose of this investigation was to evaluate associations between the timing and amplitude of quadriceps EMG activity and impulsive loading during walking gait.

Research Questions

- What is the relationship between the onset of quadriceps activity (EMG) relative to heel strike and vertical ground reaction force (vGRF) loading rate and magnitude during the first 50% of the stance phase during walking gait in individuals with ACL-R?
    - H_1: Earlier onset of quadriceps activity will be associated with lower vGRF loading rate and peak vGRF.

- What is the relationship between the amplitude of quadriceps activity prior to heel strike and vGRF loading rate and magnitude during the first 50% of the stance phase during walking gait in individuals with ACL-R?
    - H_2: Greater quadriceps activity prior to heel strike will be associated with lower vGRF loading rate and peak vGRF.

- What is the relationship between the amplitude of quadriceps activity during the load acceptance phase of walking gait and vGRF loading rate and magnitude during the first 50% of the stance phase in individuals with ACL-R?
    - H_3: Greater quadriceps activity during the load acceptance phase will be associated with lower vGRF loading rate and peak vGRF.

Chapter 2: Literature Review

ACL Injury and Epidemiology

Approximately 200,000 ACL injuries occur annually in the United States,[32] with over 50% of these traumas sustained by young athletes between the ages of 15 and 25 years.[33] ACL reconstruction (ACL-R) is by far the most common treatment strategy, with over 90% of patients opting for surgical reconstruction as opposed to rehabilitation alone.[32] For each patient undergoing ACL-R, Mather et al.[32] estimates a lifetime cost to society of $38,000. Therefore, annually, the total cost to society for ACL-R in the US amounts to $7.6 billion. Between the years 1994 and 2006, the total number of ACL reconstruction procedures increased by 50%, largely a result of the increase in procedures in patients younger than 20 years of age.[13] Published data does not support the idea that ACL-R is able to fully restore the knee to its preoperative state. In a 15-year follow-up study comparing individuals treated with ACL-R to those who were treated with a conservative rehabilitation program, nearly 60% of individuals in both groups were classified as abnormal or severely abnormal based on knee rotational instability, extension deficits, flexion deficits, and radiological OA grade.[4] It has been reported that only 31% of individuals regain normal gait patterns after ACL-R.[34] While ACL-R does successfully limit anteroposterior translation of the tibia, it does not adequately limit tibial rotation.[35] Importantly, less knee extension during gait and muscular weakness have been documented in individuals following ACL-R.[36] Changes in knee joint kinematics and altered muscle function during gait likely put individuals at risk of developing OA following ACL-R. Numerous studies have documented a heightened risk of knee OA following ACL-R.[3-10] In fact, degenerative changes in cartilage observable via MRI have been reported as early as one year following surgical reconstruction.[9] After a period of 10 to 15 years following ACL-R,

radiographic knee OA was detected in 71% of individuals, with 24% showing moderate or severe radiographic OA.[37] In addition to the high costs associated with ACL injury, this increased risk of OA development causes an even greater healthcare burden.

Knee Osteoarthritis Epidemiology

In the United States, approximately 27 million people are affected by OA.[38] This amounts to an aggregate annual healthcare expenditure of $185.5 billion,[39] at an average cost of $5,700 per year for each individual.[40] However, while the financial burden placed on those affected by OA is notable, the disabling effects of the disease are even more substantial. As knee OA is a disease of a weight-bearing joint, it has great impact on function, and often results in difficulty performing activities of daily living such as walking, stair climbing, bathing, or using the bathroom.[41] In fact, knee OA accounts for difficulty climbing stairs and walking more than any other disease.[42] Nearly 45% of individuals with symptomatic knee OA have at least some difficulty walking a quarter mile, and 42% have extreme difficulty or are unable to perform activities that require kneeling or crouching. Furthermore, 15% of individuals with knee OA use an assistive device to walk.[43] Surgery is a common treatment option, but can be an emotionally stressful event as well as a potentially dangerous form of therapy. In 2009, there were over 620,000 hospital discharges associated with total knee replacements in the United States,[44] with OA being the most common cause for treatment.[41] The effects of knee OA are multidimensional, and are not limited to physical disability. A study by Salaffi et al.[45] showed that the disease significantly affects individuals' mental and social health. The pervasive effects of this illness emphasize the importance of establishing effective prevention methods, especially among

individuals who are known to be at higher risk, such as those suffering injury to the structures of the knee.

Post-traumatic Osteoarthritis

OA is defined as a multifactorial disease, mainly resulting from the degeneration of articular cartilage. Under normal, healthy conditions, articular cartilage is smooth and lubricates the articular surfaces of bones to provide for low-friction joint movements. It additionally acts to distribute mechanical loading, protecting the bone from damaging levels of stress. Because it is avascular, there is little the body can do to self-repair or regenerate articular cartilage following injury. Symptomatic OA usually includes, but is not limited to, joint pain, inflammation, and limited range of motion.[18] The Kellgren-Lawrence scale is the most widely used OA classification and has been adopted by the World Health Organization as standard for evaluation of OA for epidemiologic studies. As it is based on the presence of osteophytes and joint space narrowing, the scale allows for good comparison between different types of joints. Kellgren-Lawrence scores range from 1 – 4, with "1" representing minute osteophyte of doubtful significance, "2" representing definite osteophyte, but joint space unimpaired, "3" representing moderate diminution of joint space, and "4" representing greatly impaired joint space and subchondral sclerosis.[46] In addition to the Kelgren-Lawrence scale, alternative methods of OA diagnosis, such as MRI, have also been utilized and supported as providing reliable and valid classifications.[47]

In contrast to idiopathic OA in which the cause is non-specific, post-traumatic osteoarthritis (PTOA) results from joint trauma associated with impact loading of the synovial joint, meniscus, capsule, or ligament tears, joint dislocation, or a combination of these injuries.

Following ACL-R, the risk for developing OA in the injured knee has been found to be 57%, compared to only 18% in the contralateral knee.[48] In the United States, lower-extremity PTOA generates an economic burden of $11.79 billion annually. Furthermore, approximately 10% of all incidences of symptomatic knee OA result from joint trauma as opposed to natural means. Of particular concern, individuals with PTOA of the knee are 10.4 years younger on average than individuals with idiopathic OA, and must face the debilitating effects of OA for a greater portion of their lives.[12] As the literature reveals a strong correlation between joint injury and OA, effective preventative interventions must be developed and implemented following injury, regardless of the presence of symptoms. By the time PTOA individuals are symptomatic, there is already irreversible damage to the articular cartilage.[49]

Gait Biomechanics Adaptations Following ACL-R

ACL-R following joint injury does not seem to restore the knee to its pre-injury state, as investigations have revealed adaptations to gait biomechanics that may predispose the articular cartilage to future degeneration. It has been reported in the literature that ACL-R knees are deficient in knee extension[36] and exhibit less hip and knee flexion during gait.[50] In an investigation of gait kinematics, 85% of subjects displayed more external rotation of the tibia in the ACL-R knee compared to the contralateral knee at HS and during the midstance, terminal extension, and toe off phases of gait.[51] Papannagari et al.[52] found that reconstructed knees showed more anterior tibial translation and external rotation during weight bearing tasks. Other studies have contradictorily noted more internal rotation in ACL deficient knees during gait.[53] Furthermore, some literature reports significantly reduced peak knee extension at HS in the ACL-R knee compared to the contralateral knee.[54] In a healthy knee joint, the thickest regions of

the femoral and tibial articular cartilage align when the knee is extended, as it is prior to HS. It has been suggested that the locations of the regions of thick articular cartilage are tibiofemoral adaptations to help alleviate the impact loading that occurs at HS.[55] As such, kinematic changes following ACL-R result in a shift in the areas of contact of the articular cartilage such that there is increased loading in areas of cartilage not conditioned for extensive weight bearing.[56] This shift in areas of cartilage contact provides a potential explanation for the relationship between ACL-R and OA development.

In addition to the gait kinematic alterations that have been reported following ACL-R, the literature shows several kinetic changes as well. During a stair climbing exercise, individuals with ACL-R relied more heavily on hip extension moments, as they displayed a 22% decrease in peak knee extension moments. Such alterations have been suggested to result from greater quadriceps and hamstring co-contraction, subjecting the articular cartilage to increased compressive loading.[57] Additionally, greater knee adduction moments during gait have been observed in the injured and contralateral limbs of ACL-R subjects relative to control subjects.[58,59] This is cause for concern as greater external knee adduction moment, a measure of loading in the medial compartment of the knee, has been reported to highly correlate with OA progression.[60] Some studies, however, have found ACL-R individuals to display similar or decreased external knee adduction moment,[61,62] demonstrating the variability of individuals' gait patterns following ACL-R. The discrepancies in these investigations (i.e. some ACL-R subjects display altered gait kinetics while others do not) may parallel differential development of knee OA.

Ground reaction forces are indicative of lower extremity loading and are useful proxies for dynamic joint loading during gait. Specifically, the vertical component of the ground reaction force provides an estimate of the axial forces sustained by the articular cartilage of the knee joint.

Chen et al.[63] provided evidence that the extent of damage to articular cartilage is dependent on peak stress, stress rate, and loading duration by subjecting canine cartilage to repetitive impacts. Even when peak stress was low (2.5 MPa) and administered for a duration of only 2 minutes, damage to the cartilage matrix was observed at high stress rates, suggesting that loading rate is highly correlated with cartilage degeneration. Furthermore, impact stresses resulted in more damage than did smoothly arising compressions at the same peak stress level. In a study of bovine knee articular cartilage, higher rates of loading resulted in matrix damage characterized by longer fissure length and greater fissure depth compared to low loading rates.[64] In damaged articular cartilage, cyclic loading has been shown to propagate fissure length in vitro, suggesting a potential mechanism of OA progression related to repetitive loading in gait.[65] In addition to the mechanical damage to articular cartilage associated with high loading rates, Kurz et al.[66] found decreases in the biosynthetic activity of cartilage following high rate impact loading. In the healthy joint, cartilage responds to low-amplitude cyclic loading with an anabolic response. Deficient anabolic activity following high rate loading may provide further explanation regarding the pathogenesis of PTOA.

In a cohort of females, Noehren et al.[67] found that average loading rates and initial impact forces during walking and running were significantly higher in the ACL-R group compared to control. Due to the repetitive and perpetual nature of gait, slight increases in impact loading could result in significant consequences for the articular cartilage. Because higher impact loading was found during walking, this suggests that ACL-R individuals experience greater cartilage loading during daily activities, not just during sport or exercise. Of additional concern is the lack of between-limb differences, suggesting that gait adaptations following ACL-R could increase the risk of joint injury bilaterally. This data is consistent with findings from a smaller cohort of

individuals with ACL-R, which found higher levels of impulsive loading in both extremities of ACL-R individuals compared to both extremities of controls.[68] Contrary to studies showing no between-limb differences in loading rates, a more recent study by Blackburn et al.[69] found significantly higher instantaneous loading rates in ACL-R limbs. Likewise, instantaneous loading rates were higher in individuals characterized as "impulsive loaders," who commonly displayed high peaks in vertical ground reaction force at HS. Greater loading rate has been identified as a common gait characteristic in individuals with knee OA, suggesting a link between ACL-R and OA development.[28] Using MR imaging, Morgenroth et al.[26] found an independent relationship between dynamic loading rate and degeneration of the medial knee cartilage in vivo. As evidence suggests that high loading rates can significantly damage articular cartilage even at small magnitudes, interventions targeted at preventing increased rates of loading following ACL-R could inhibit cartilage degeneration and the development of PTOA.

Quadriceps Influence on Loading Rate

During gait, the quadriceps play an important role in controlling the limb prior to HS and managing contact forces during loading. Eccentric action of the quadriceps is responsible for controlling knee flexion as a way of attenuating the large magnitude of force that is transferred to the limb during the load acceptance phase of gait.[21] Decreased quadriceps activity during gait may result in higher loading rates due to the diminished utilization of eccentric action to absorb shock. Jefferson et al.[23] showed that inhibition of the quadriceps caused by injecting lidocaine in the femoral nerve invokes impulsive loading in individuals with normal gait patterns. When the quadriceps were inhibited, subjects displayed increased vertical foot velocity prior to ground contact, providing evidence that under normal conditions, the quadriceps decelerate the limb

prior to HS as a way of reducing high rate loading. In a group of healthy subjects, Verdini et al.[22] found that 100% of subjects with delayed activation of the vastus medialis displayed impulsive loading during gait. Whereas those with normal gait patterns used quadriceps activity at the end of the swing phase to decelerate the limb and prepare for ground contact, individuals with delayed activation likely relied on the ground to abruptly decelerate the limb. Repetitive loading in this manner may accelerate damage to the articular cartilage. Lewek et al.[21] found that individuals with quadriceps strength deficits after ACL-R exhibited movement patterns similar to ACL deficient patients. The individuals with weak quadriceps exhibited reduced knee flexion, thus inhibiting force attenuation during the load acceptance phase. In a cohort of women, Mikesky et al.[25] further emphasized the importance of the quadriceps during gait, reporting much higher loading rates in individuals with weaker quadriceps compared to a group of strength-trained women. Likewise, in individuals with knee OA, lower preparatory activity of the quadriceps has been associated with impulsive loading.[17] As ACL-R limbs have been observed to display greater magnitude loading rates compared to the contralateral limb,[69] diminished quadriceps activity after ACL injury may be a viable target for interventions aimed at preventing PTOA.

Quadriceps EMG after ACL Injury

Surface electromyography (EMG) is an easy, non-invasive method of quantifying muscle activity during static or dynamic tasks. Through the use of electrodes, surface EMG produces a signal based on the sum of the nearby motor unit action potentials (MUAP) that are transmitted during contraction. While the EMG signal is not equivalent to muscle force, it is indicative of the recruitment of MUAPs and their firing frequency. As such, it can be used to determine the timing

of muscle activation as well as the patterns and strength of the neuromuscular signaling for a given muscle.[70]

Following ACL-R, studies involving EMG have revealed alterations in quadriceps activity. In an animal model, altered EMG patterns during the loading phase of gait were directly associated with transection of the ACL.[71] Torry et al.[72] observed decreases in quadriceps activity during gait with increasing levels of joint effusion, providing evidence that knee injury is associated with quadriceps dysfunction. At high levels of knee joint effusion (80 cm^3), vastus medialis EMG activity decreased by 25% while rectus femoris activity decreased by 50.4 %. While the literature concerning quadriceps EMG activity during gait is limited in individuals with ACL-R, Hurd et al.[73] reported significant reductions in EMG activity of the quadriceps during the load acceptance phase of gait in a cohort of ACL-R individuals. This is cause for concern as individuals with knee OA who display impulsive loading have been found to exhibit 43.5% lower pre-activity of the quadriceps.[17] The lack of quadriceps activity prior to HS was associated with peak forces at the start of the loading phase of gait, regardless of walking speed. Furthermore, it has been reported that individuals with knee OA activate their quadriceps significantly later than controls during other functional tasks as well, such as stair descent.[74] Altered EMG activity of the quadriceps during normal activity may contribute to greater loading rates and the progression of cartilage degeneration. Because ACL-R individuals display quadriceps EMG patterns similar to those who suffer from knee OA, decreased quadriceps activity during gait may serve as a mechanism for the development of PTOA.

EMG Processing during Gait

There is no consensus among the literature regarding the best method for processing EMG signals. In studies involving EMG during gait, it is common for the signal to be full-wave rectified (taking the absolute value of the EMG signal) and filtered to produce a linear envelope.[75-78] The linear envelope is a processed form of the raw EMG data that reduces noise to provide more useful results for analysis. However, upon obtaining this more useful output, methods for determining EMG amplitude and muscle onset are varied. It should be noted that many investigations fail to provide detailed explanations of the methodology used to evaluate EMG data, further complicating the selection of an ideal protocol.[79] In a previous investigation of gait parameters in ACL-R individuals, Alkjaer et al.[75] calculated mean amplitude during the weight acceptance period from 100ms prior to HS to the first peak on the vGRF curve. Theoret et al.[76] quantified muscle activation by calculating the area under the curve of the linear envelope for each participant's average running cycle (from heel strike to heel strike). Tang et al.[78] utilized a different method, calculating root mean square (RMS) values in a 20ms smoothing window throughout the gait cycle. To determine preparatory activity of the quadriceps, peak RMS EMG values were obtained for the 200ms interval prior to HS. Furthermore, most EMG data in the literature is normalized for each individual based on a selected reference activity. Multiple studies have normalized all signals obtained during gait to the maximal EMG amplitude recorded during a maximal voluntary isometric contraction for the muscle group of interest.[17,75,78] Others, however, have normalized signals to the average of the peak EMG signal among multiple gait trials.[77] For the present study, it seems suiting to use EMG processing methodology similar to that of Liikavainio et al.,[17] who conducted a closely related study in individuals with knee OA. Quadriceps pre-activity was defined as the average EMG activity level throughout the 100ms

time interval prior to HS. All data was normalized to the average EMG values of the quadriceps during maximal voluntary isometric contraction.

In regards to the determination of muscle onset, investigations have utilized protocols based on visual determination, computer assistance, and fully automated algorithms.[80] Theoret et al.[76] first determined a noise level of the signal by selecting a period of the gait cycle when the muscle was not active, then set a threshold for onset of the contraction at two standard deviations higher than the resting value. Similarly, Tang et al.[78] used an algorithm that determined onset when the signal differed by three standard deviations. To determine the validity of different methods for determining muscle onset, Hodges et al.[79] compared the onset times determined by numerous computer-based algorithms to the onset times determined by an experienced examiner. The study compared twenty-seven different combinations of parameters, with each algorithm differing in regards to the degree of smoothing (low pass filter), the number of samples assessed in the sliding window (20, 50, or 100), and the magnitude of the deviation from baseline activity required to indicate muscle onset (threshold value). Based on the results, multiple algorithms proved relatively valid, but the most accurate algorithm used a 50 Hz low pass filter, threshold level of 1 standard deviation above baseline, and a 100-sample sliding window (50ms epoch).

Summary

ACL injury is prevalent in the US and is becoming more frequent among younger populations. This is of concern as ACL injury, despite reconstructive surgery, is highly associated with the development of PTOA in the literature. ACL-R does not restore the knee to its pre-operative state, as the literature reports gait kinematic and kinetic alterations that persist years after surgical intervention. Altered muscle function after injury may play a role in the

alterations observed during gait, and dysfunction of the quadriceps specifically may serve as the mechanism for greater loading rates in ACL-R individuals. Without proper quadriceps activation timing and activation amplitude both prior to HS and throughout the load acceptance phase of gait, individuals with ACL-R may be subject to repetitive, impulsive loading. Such loading has proven to be independently damaging to articular cartilage. Therefore, understanding the relationship between quadriceps activity and loading rate could divulge a viable target for interventions aimed at preventing the development of OA after ACL injury.

Chapter 3: Methods

Subjects

Nine individuals were recruited from two local orthopaedic clinics (UNC Department of Orthopaedics and Triangle Orthopaedic Associates), rehabilitation clinics, the University population, and the Durham Veterans Affairs Medical Center. Subjects were included if they were between the ages of 18-35 years and had undergone unilateral ACL-R within 5 years, but no less than 6 months prior to participation. Exclusion criteria included a history of ACL graft rupture or revision surgery, a history of neurological disorder, or a history of injury to either leg within 6 months prior to participation. Furthermore, central activation ratio was assessed to ensure that subjects possessed deficits in quadriceps function in the ACL-R limb (<95%). Likewise, the Knee Injury and Osteoarthritis Outcome Score (KOOS) self-report survey was used to ensure that subjects were functional enough to complete the study requirements. To be included, subjects were required to score greater than 53.1 on the KOOS Pain subscale, and greater than 44.9 on the KOOS Symptom subscale. Lastly, subjects had to have been cleared by a physician for return to physical activity, and currently physically active, participating in at least 20 minutes of physical activity 3 times per week. During the screening session on the first day, subjects were evaluated for the inclusion criteria and required to read and sign an informed consent form prior to data collection. (See Table 1 for subject demographics)

Experimental Design

This project was a part of a larger ongoing investigation evaluating the effects of vibratory stimuli on factors linked to OA in individuals with ACL-R. The overarching investigation utilizes a single-blind randomized controlled experimental design consisting of a

convenience sample of 75 individuals who had undergone ACL-R. It includes assessments of quadriceps function outcomes (peak voluntary torque, rate of voluntary torque development, and the central activation ratio), proprioception/sensory outcomes (joint repositioning assessment and vibratory perception threshold), and gait biomechanics outcomes (kinematics, kinetics, and EMG variables). Subjects complete the aforementioned assessments prior to and following vibratory interventions designed to enhance quadriceps activity.

The present investigation was cross-sectional, and evaluated the relationship between quadriceps activity and loading rates during gait using data obtained from the baseline assessments. While the larger study required subjects to complete 3 testing visits, the present study only included data collected during the first 2 visits to the Sports Medicine Research Lab at the University of North Carolina at Chapel Hill. Data obtained during the screening session on the first day was used to ensure that subjects met all inclusion criteria. On the second visit, subjects completed the gait biomechanics assessment.

Gait Biomechanics Assessment

During the screening session, subjects performed 5 walking trials along a 6-meter walkway. Subjects walked barefoot at a self-selected pace and gait speed was monitored using infrared timing gates. Using the 5 trials during the screening session, an average preferred gait speed was recorded for each participant. Subjects completed 5 walking trials for which gait speed was within +/- 5% of the preferred speed and the entire foot made contact on each force plate. Trials that did not meet these criteria were repeated.

Vertical ground reaction forces were measured using two force plates (model 4060, Bertec Corp., Columbus, OH) embedded in the walkway and staggered such that kinetic data

could be recorded for both limbs in a single trial. Loading rate was assessed using the vGRF data obtained from the force plates. Ground reaction forces were sampled at 1,200 Hz and low-pass filtered at 75 Hz. Outcome variables included the peak vGRF during the first 50% of the stance phase, linear loading rate (slope of the line connecting HS and peak vGRF during the first 50% of the stance phase), and the peak instantaneous loading rate (1^{st} time derivative). The stance phase was defined as the interval from HS (vGRF $\geq$ 20N) to toe off (vGRF $\leq$ 20N). All vGRF magnitudes and loading rates were normalized to body weight (xBW and xBW/s, respectively).

EMG data was sampled during each of the 5 trials at 1,200 Hz using surface EMG (DelSys Bagnoli-8; Input Impedance: 1.0 MΩ; EMG100C Amplifiers, CMRR: 110 dB min, gain: 10000). Preamplified EMG electrodes were placed on the vastus medialis and vastus lateralis of each limb. The electrode sites were shaved if necessary, and skin was abraded and cleaned with alcohol to improve the quality of the signal. The raw EMG signal was bandpass (20-350 Hz) and notch (59.5-60.5 Hz) filtered (4^{th} order zero-phase lag Butterworth filter). Signal smoothing was accomplished using a low pass filter at 10Hz to create a linear envelope.

Quadriceps EMG variables of interest included the onset of activity prior to HS, preparatory activity of the quadriceps prior to HS, and the amplitude of activity during the loading phase. The onset of quadriceps activity was defined as the point prior to HS at which the EMG amplitude exceeds the mean amplitude of a selected 100ms quiet period (quiet mean) during the gait cycle plus 2 SD for at least 120ms. Quadriceps preparatory activity was quantified in two ways: firstly, by calculating the mean EMG amplitude from muscle onset to HS, and secondly, by calculating the mean EMG amplitude during the 100ms prior to HS. Lastly, quadriceps activity during the loading phase was quantified by calculating the mean

EMG amplitude from HS to the peak vGRF during the first 50% of the stance phase. All mean EMG amplitudes were normalized to the quiet means for each respective trial.

Statistical Analyses

Partial correlations (Pearson r) were used to evaluate the relationships between each EMG variable (quadriceps onset, pre-activity, and loading phase activity) and loading variable (peak vGRF, vGRF linear and instantaneous loading rates) after controlling for gait speed. The strength of the associations will be interpreted according to the r value, with values from 0.00 to 0.25 representing little or no relationship, 0.25 to 0.50 representing a fair relationship, 0.50 to 0.75 representing a moderate to good relationship, and above 0.75 representing a good to excellent relationship.[81] Analyses were conducted with an *a priori* alpha level of 0.05.

Table 1 **Subject Demographics**

N	Age (years) ± SD	Height (cm) ± SD	Weight (N) ± SD	Time Since Injury (months) ± SD	Time Since Surgery (months) ± SD
9 (2 male, 7 female)	19.7 ± 1.7	171.8 ± 13.3	751.4 ± 288.3	33.1 ± 13.0	30.8 ± 12.6

Figure 1. Illustration of gait biomechanics assessment

Chapter 4: Results

Two subjects were excluded from statistical analysis due to the fact that their EMG signals contained high levels of noise and did not demonstrate cyclical activity representing gait. One subject was excluded on the basis of inaccurate vGRF data. Therefore, while nine subjects completed the gait biomechanics assessment, data from six subjects was used for statistical analysis. Demographic data for the retained subjects is presented in Table 2. Additionally, due to high levels of noise in the vastus medialis EMG signals, statistical analysis was only performed using EMG data from the vastus lateralis.

VL EMG Onset

There was no significant correlation between VL EMG onset and any of the three kinetic variables: peak vGRF ($r = -0.090$, $p = 0.443$), vGRF linear loading rate ($r = 0.196$, $p = 0.376$), and vGRF instantaneous loading rate ($r = -0.573$, $p = 0.156$). (See Table 4)

VL Preparatory Activity (Onset to HS)

There was no significant correlation between mean VL EMG amplitude from onset to HS and any of the three kinetic variables: peak vGRF ($r = -0.293$, $p = 0.316$), vGRF linear loading rate ($r = -0.071$, $p = 0.455$), and vGRF instantaneous loading rate ($r = -0.637$, $p = 0.124$). (See Table 4)

VL Preparatory Activity (100ms prior to HS)

There was a significant negative correlation between mean VL EMG amplitude during the 100ms prior to HS and vGRF instantaneous loading rate ($r = -0.819$, $p = 0.045$). This indicates that subjects with greater VL activity over the 100ms interval prior to HS demonstrated lower vGRF instantaneous loading rates (See Figure 2). No significant correlation was found between mean VL EMG amplitude during the 100ms prior to HS and peak vGRF ($r = -0.415$, $p = 0.244$) or vGRF linear loading rate ($r = -0.052$, $p = 0.467$). (See Table 4)

VL Loading Phase Activity

There was no significant correlation between mean VL EMG amplitude during the loading phase any of the three kinetic variables: peak vGRF ($r = -0.445$, $p = 0.226$), vGRF linear loading rate ($r = -0.379$, $p = 0.265$), and vGRF instantaneous loading rate ($r = -0.142$, $p = 0.410$). (See Table 4)

Table 2 Demographics of Subjects Included for Analysis

N	Age (years) ± SD	Height (cm) ± SD	Weight (N) ± SD	Time Since Injury (months) ± SD	Time Since Surgery (months) ± SD
6 (1 male, 5 female)	19.2 ± 1.6	173.8 ± 11.0	765.6 ± 319.6	34.5 ± 9.2	32.8 ± 9.2

Table 3 Descriptive Statistics (mean ± SD)

VL EMG Onset (ms before HS)	VL Pre-activity from Onset to HS (% quiet mean)	VL Pre-activity 100ms before HS (% quiet mean)	VL Loading Phase Activity (% quiet mean)	Peak vGRF (xBW)	vGRF Linear Loading Rate (xBW/s)	vGRF Instantaneous Loading Rate (xBW/s)
111.64 ± 40.83	2.98 ± 0.86	2.99 ± 1.13	5.62 ± 2.57	1.12 ± 0.40	7.80 ± 1.73	62.99 ± 29.40

Table 4 Partial Correlations between Quadriceps Activity Measures and Gait Kinetics in the ACLR Limb

	Peak vGRF	vGRF Linear LR	vGRF Instantaneous LR
VL Onset	-0.090	0.196	-0.573
Preparatory VL Activity (100ms)	-0.415	-0.052	**-0.819***
Preparatory VL Activity (onset to HS)	-0.293	-0.071	-0.637
Loading Phase VL Activity	-0.455	-0.379	-0.142

Partial correlations reflect relationships between the respective quadriceps activity measures and loading variables after accounting for the influence of gait speed. * $p < 0.05$

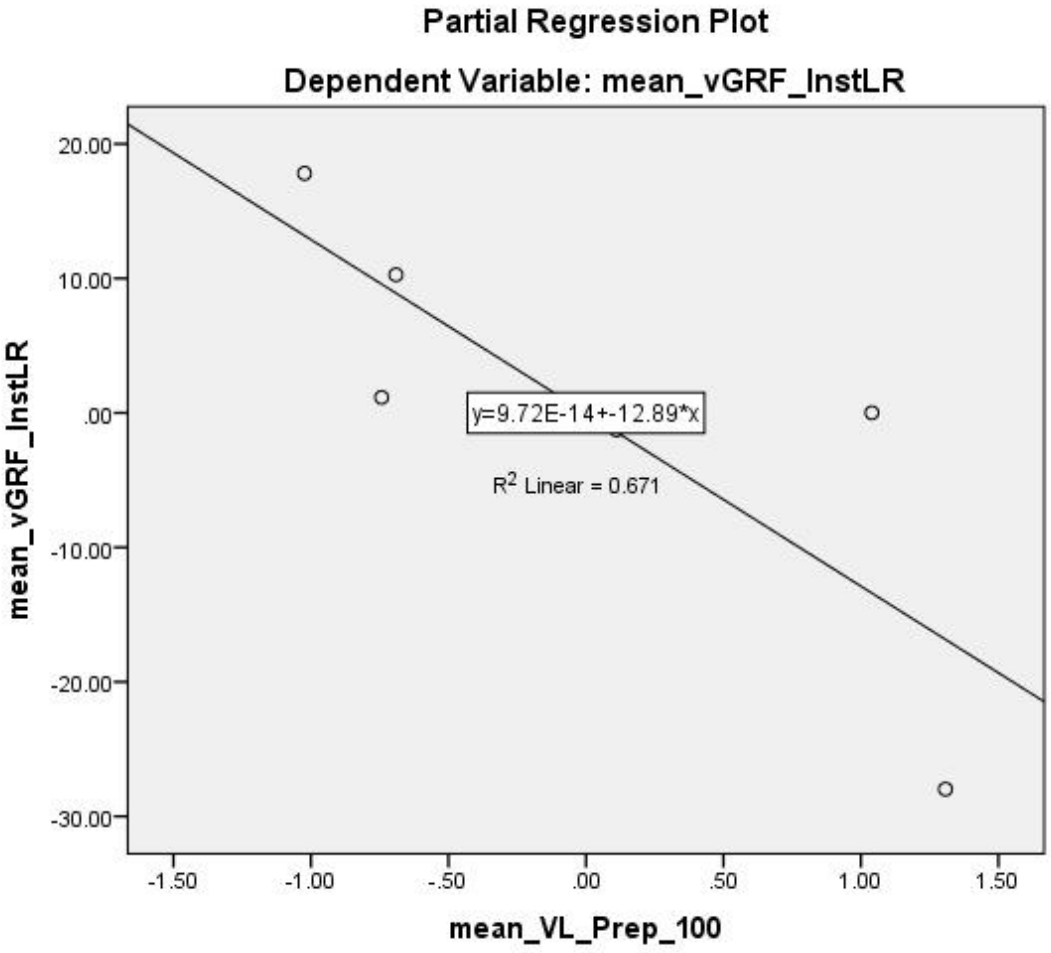

Figure 2. Regression plot of mean preparatory VL activity during the 100ms prior to HS and mean vGRF instantaneous loading rates after controlling for gait speed.

Chapter 5: Discussion

The primary finding of this study was that greater activity of the VL during the 100ms prior to HS was associated with lower vGRF instantaneous loading rates in the ACL-R limb during gait. This is consistent with previous research that demonstrates the importance of the quadriceps in attenuating impact forces during gait,[23] and builds on these findings by clarifying how muscle activity alters loading during gait. Activity of the VL during the 100ms prior to HS was not associated with peak vGRF or linear loading rate. Other measures of quadriceps activity, including timing of EMG onset, preparatory activity from onset to HS, and VL activity during the loading phase, were not associated with peak vGRF, linear loading rate, or instantaneous loading rate. Thus, findings from this study are only partially consistent with the experimental hypotheses. It was hypothesized that earlier onset of the quadriceps, greater quadriceps activity during the loading phase and greater preparatory activity both during the 100ms preceding HS and from onset to HS would result in lower peak vGRF, linear loading rate, and instantaneous loading rate. Our findings suggest that quadriceps activity immediately prior to HS (specifically during the preceding 100ms) influences vGRF instantaneous loading rate, and may be an important target for interventions aimed to reduce impulsive loading following ACL-R.

Blackburn et al.[69] found that peak vGRF and linear loading rate did not differ between the ACL-R limb and the contralateral limb during gait, but instantaneous loading rate was significantly higher in the ACL-R limb. Additionally, instantaneous loading rates, but not linear loading rates or peak vGRF, were significantly greater in individuals classified as impulsive loaders compared to normal loaders. This suggests that changes in loading associated with ACL-R may not be detectible via measures such as vGRF linear loading rate and peak vGRF. Linear loading rate is displayed in Figure 2 by the dashed line connecting HS to peak vGRF. This

calculation is based on data from HS to peak vGRF, and is not influenced by the sharp rise in vGRF immediately following HS (represented by point "a" in Figure 3). Likewise, peak vGRF is not influenced by the sharp rise in vGRF immediately following HS. Peak instantaneous loading rate is a measure of the maximum slope at any point on the vGRF curve, which usually occurs during the first 20ms following HS.[69] Thus, instantaneous loading rate provides a representation of kinetics directly following HS, and is a better indicator of the impulsive loading thought to damage articular cartilage. As such, our finding that greater preparatory activity of the quadriceps is associated with lesser instantaneous loading rates supports that notion that appropriate quadriceps activity is critical for regulating impulsive loading that is hypothesized to lead to knee OA.

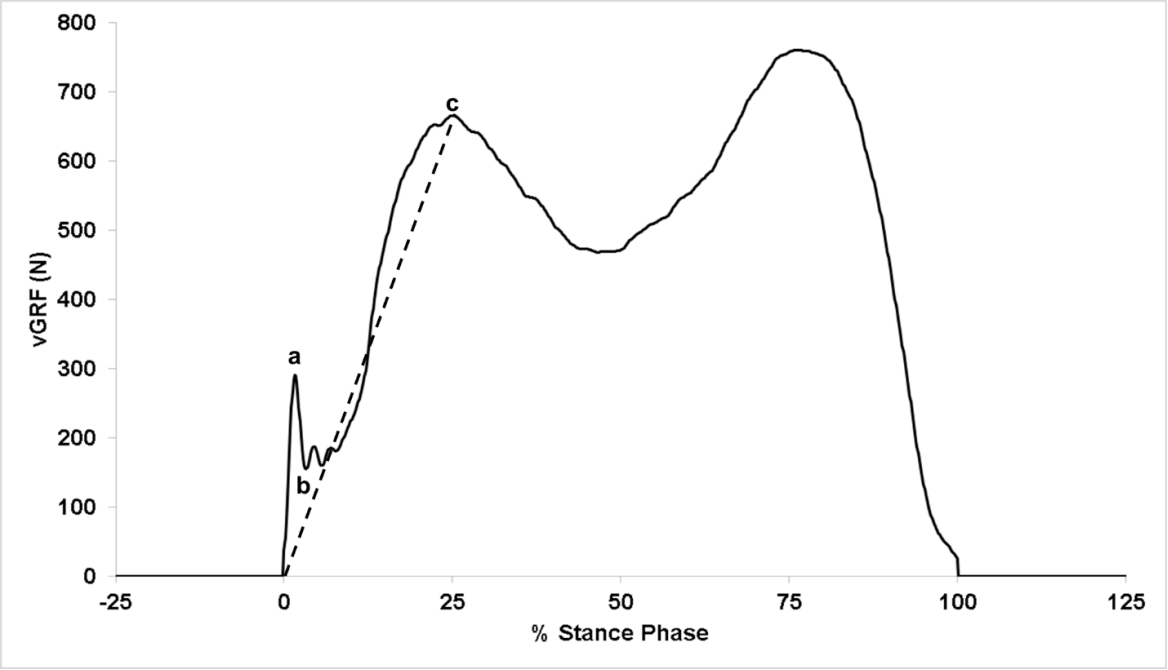

Figure 3. Typical vGRF curve during walking gait

The lack of association between onset of quadriceps activity and the loading variables is inconsistent with research showing that delayed muscle activation may result in increased impact forces.[22] A potential explanation for this discrepancy could be due to difficulties identifying onset times in the present study. The method for identifying muscle onset utilized a mean EMG amplitude from a 100ms quiet interval during the gait trial. Onset was identified when EMG amplitude exceeded the mean plus two standard deviations for a burst duration of 120ms at any point following the selected start time for the quiet interval. In many trials, the EMG signal was noisy prior to HS, making it difficult to select an interval of 100ms where the muscle appeared to be quiet. Therefore, the quiet mean was likely artificially high in some trials, compromising the validity of the detected onset times. Additionally, some level of subjectivity was introduced when detecting onset. Depending on which quiet period was selected, the onset time could vary significantly. The limitation in reliably and accurately detecting quadriceps onset affected the measure of preparatory quadriceps activity from onset to HS as well. This method of quantifying preparatory muscle activity was dependent on the onset time, and is likewise limited in its validity. Future studies should alter onset detection methods, potentially establishing the threshold level based on a mean EMG amplitude during a quiet stance period instead using a quiet period from each gait trial.

Another important finding of this study was that quadriceps activity during the loading phase was not associated with peak vGRF, linear loading rate, or instantaneous loading rate. Loading phase activity quantifies quadriceps activity from HS to the peak vGRF during the first 50 percent of the stance phase. One possible explanation for the observed results is that preparatory activity of the quadriceps is more important in attenuating loading rates than activity that occurs after HS. The maximum instantaneous loading rates usually occur within 20ms

following HS. However, loading phase activity is an average EMG amplitude over an approximately 200ms interval, from HS to peak vGRF.[69] Since the majority of loading phase activity occurs after the time point when maximal instantaneous loading rates occur, it is not surprising that these two variables are not significantly correlated.

Previous research by Liikavainio et al.[17] is consistent with the findings of the present study, showing that preparatory activity of the quadriceps during the 100ms preceding HS influences loading during walking gait. Liikavainio et al. found that lower pre-activity of the quadriceps was associated with impulsive loading in individuals with osteoarthritis. Calculating preparatory activity in this way, as opposed to utilizing muscle onset, avoids the bias and detection errors associated with identifying muscle onset, potentially explaining the correlation outcomes when using this method. Another potential explanation is that activity within 100ms prior to HS may have a greater influence on loading immediately following HS compared to quadriceps activity earlier in the swing phase.

It should be noted that several moderate correlations were observed that did not achieve significance, potentially due to the small sample size of the present study. Greater instantaneous loading rate was moderately correlated (i.e. $r \geq 0.50$) with later onset of the quadriceps ($r = -0.573$, $p = 0.156$) and lower preparatory activity of the quadriceps from onset to HS ($r = -0.637$, $p = 0.124$).[81] A larger sample size and improved methodology for reliably identifying muscle onset could result in significant correlations between these variables. If future observations were to identify greater instantaneous loading rates to be significantly correlated with later onset and lower preparatory activity of the quadriceps from onset to HS, this would complement the present finding regarding the significance of quadriceps activity during the 100ms prior to HS.

As knee osteoarthritis is evident as early as one year following ACL-R,[9] it is imperative to identify and address the underlying deficiencies contributing to cartilage breakdown. Evidence suggests that high rate loading is independently damaging to articular cartilage,[26,63] and can inhibit its biosynthetic activity.[66] Noehren et al.[67] found that individuals with ACL-R had higher average loading rates during gait compared to controls, and Blackburn et al.[69] found that instantaneous loading rates were significantly greater in the ACL-R limb versus the contralateral limb. The present findings suggest that lower quadriceps activity 100ms prior to HS in ACL-R limbs is correlated with higher instantaneous loading rates. Therefore, future research should evaluate interventions aimed to increase preparatory activity of the quadriceps during gait in individuals with ACL-R. In a previous investigation, Verschueren et al.[82] used vibration of the patellar tendon to significantly increase quadriceps EMG activity during gait in healthy individuals. By attaching a cylindrical vibrator to the tendon using a rubber band, mean EMG across the complete gait cycle was found to increase by 69% in the rectus femoris and 65% in the vastus lateralis when compared to mean EMG values during trials with no vibration. Similarly, Cotey et al.[83] observed increased quadriceps activity during gait in healthy individuals and individuals with neurological injury through the use of vibration. By strapping the vibration device over the anterior thigh, mean EMG area increased by 96% in the rectus femoris and by 211% in the vastus lateralis compared to the control condition (no vibration). Interestingly, phase specific increases in quadriceps activity could be invoked when the vibration was only applied to specific periods of the gait cycle. Mean EMG area in the vastus lateralis increased by 123% during the swing phase and by 100% during the transition into stance phase when phasic vibration was applied to healthy individuals. Further research should investigate whether similar methodologies elicit greater preparatory activity of quadriceps in individuals with ACL-R.

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