

**KNEE FUNCTIONAL RECOVERY AND LIMB-TO-LIMB SYMMETRY
RESTORATION AFTER ANTERIOR CRUCIATE LIGAMENT (ACL)
RUPTURE AND ACL RECONSTRUCTION**

by

Zakariya Hussein Nawasreh

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

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Zakariya Hussein Nawasreh

Approved: _____
Charles Swanik, Ph.D.
Chair of the Department of Biomechanics and Movement Science

Approved: _____
Kathleen S. Matt, Ph.D.
Dean of the College of Health Sciences

Approved: _____
James G. Richards, Ph.D.
Vice Provost for Graduate and Professional Education

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Signed:

Lynn Snyder-Mackler, PT, ATC, SCS, Sc.D, FAPTA
Professor in charge of dissertation

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed:

David Logerstedt, PT, Ph.D., MPT, SCS
Professor in charge of dissertation

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed:

Michael J. Axe, MD
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed:

Karin Silbernagel, PT, Ph.D., ATC
Member of dissertation committee

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ABSTRACT

Anterior cruciate ligament (ACL) rupture is a common sport injury of young athletes who participate in jumping, cutting, and pivoting activities. Although ACL reconstruction (ACLR) surgery has the goal of enabling athletes to return to preinjury activity levels, treatment results often fall short of this goal. The outcomes after ACLR are variable and less than optimal with low rate of return to preinjury activity level and high risk for second ACL injury. Factors related to the knee functional limitations, strength deficits, and limb-to-limb movement asymmetry may be associated with poor outcomes after ACLR. Additionally, the criteria that are used to determine a patient's readiness to return to the preinjury activity level are undefined which may also be associated with poor outcomes after ACLR.

The clinical decision-making to clear patients' for safe and successful return to high physical activities should be based on a universal comprehensive set of objective criteria that ensure normal knee function and limb-to-limb symmetry. A battery of return to activity criteria (RTAC) that emphasizes normal knee function and limb-to-limb movement symmetry has been constituted to better ensure safe and successful return to preinjury activity level. Yet, only variables related to patients' demographics, concomitant injuries, and treatment measures have been used to predict return to preinjury activity levels after ACLR. However, the ability of RTAC variables that ensure normal knee function and limb movement symmetry to predict the return to participate in the same preinjury activity level after ACLR has not been investigated. In light of this background, the first aim of the present study was to compare functional knee performance-based and patient-reported measures of those who PASS and who FAIL on RTAC at 6 months (6-M) following ACLR with those at 12 months

(12-M) and 24 months (24-M) following ACLR and to determine how performance-based and patient-reported measures change over time. Further to investigate whether RTAC variables at 6-M following ACLR predict return to the same preinjury activity level at 12 and 24 months following ACLR.

The findings of this work revealed that patients who fail on RTAC 6-M after ACLR are more likely to demonstrate impaired knee function and limb-to-limb movement asymmetry at 12-M and 24-M after ACLR. Additionally, RTAC variables can predict the return to participate in the same preinjury activity level at 12-M and 24-M after ACLR. The combination of RTAC variables explain more than one-fourth to one-third of returning to participate in the same preinjury activity level 12-M and 24-M respectively after ACLR.

For athletes choosing non-surgical management, the physical therapy recommendation is to administer progressive strength training augmented with manual perturbation training. Manual perturbation training is a type of specialized neuromuscular training that includes purposeful manipulations of support surfaces by a therapist. While manual perturbation promotes dynamic knee stability, enhances dynamic knee function, mitigates abnormal movement pattern and normalizes the muscle co-contraction, perturbation training is not widely used as part of the ACL rehabilitation program in the United States. Further, the perturbation training requires extensive physical labor and one-on-one time from the treating therapist. The effect of administering perturbation training using mechanical device as part of the ACL rehabilitation program has not been investigated. An automated “Reactive Agility System” device provides perturbation stimuli including multidirectional translations similar to those of manual perturbation training. Administering the perturbation training using a

mechanical device may facilitate the use of controlled and standardized training in a wide range of the rehabilitation clinics and allow administering controlled and standardized training. However, it is unknown whether administering perturbation training using mechanical device provides effects similar to manual perturbation training on knee mechanics, knee functional performance, and neuromuscular activation pattern in patients with ACL rupture. The second aim of this study was to measure whether the mechanical perturbation training provides an effect similar to that of manual perturbation training on gait mechanics, knee functional performance, muscle co-contraction, and neuromuscular activation pattern in athletes with an acute ACL rupture who are managed non-surgically. The findings of this work revealed that mechanical perturbation training provides effects similar to the manual perturbation training on knee kinematics and kinetics during walking and performance-based and patient-reported measures. Gait limb-to-limb asymmetries continue persist after the training regardless of the treatment group which may indicate that patients require participating in an extended rehabilitation program. Additionally, Perturbation training attempts to resolve the neuromuscular deficits and restore a balance in muscle activation and strength between knee flexors and extensors to enhance the dynamic stability of the knee joint. There are moderate to strong relationships between time duration of muscles' activities and the muscle co-contraction that may reflect neuromuscular adaptations to provide dynamic knee stability.

Chapter 1

INTRODUCTION

In the United States, approximately a quarter of a million anterior cruciate ligament (ACL) ruptures occur annually¹. ACL ruptures occur commonly among young athletes who participate in sport activities that include jumping, cutting, and pivoting maneuvers². The ACL rupture is a devastating injury causing structural and functional deficits^{3,4}. After ACL rupture, only some individuals can successfully achieve dynamic knee stability during high demand functional activities^{5,6}. Most individuals, however, exhibit dynamic knee instability during basic daily living activities such as walking⁷⁻¹⁰. As a result, individuals with ACL rupture compensate to the increased knee laxity by altering the gait pattern and adopting abnormal neuromuscular strategies^{4,11,12}. In addition, patients with an ACL rupture experience knee impairments and functional limitations¹³⁻¹⁵. The abnormal gait pattern and functional limitations may stand as barriers that prevent athletes from returning to highly physical activities for many athletes and for some athletes may never return to the preinjury activity level¹⁶⁻¹⁸. Additionally, the presence of knee functional limitation and gait abnormalities may lead to negative consequences during the performance of dynamic functional activities^{19,20}.

The treatment options for individuals with ACL rupture including non-surgical or surgical management^{9,21,22}. The ultimate goals of non-surgical or surgical management are to restore dynamic knee stability, normal knee function, and

movement symmetry during functional activities to prevent damages to the knee structures and to facilitate returning to the pre-injury activity level.

1.1 Functional Limitations and Gait Abnormalities after ACL Rupture

Early after ACL rupture, it is common for patients to experience knee impairments and functional limitations including joint effusion, limited knee range of motion, decreased quadriceps strength, and limb-to-limb functional asymmetry^{19,23-27}. Additionally, some patients exhibit multiple episodes of dynamic knee instability during participation in simple to high physical activities²⁸. Some functional limitations (i.e. quadriceps strength deficit) continue to persist for months after ACL rupture and years after reconstruction surgery^{29,30}. Unresolved knee impairment and functional limitations after ACL rupture have negative impacts on the patients' functional performance and prevent them from return to the preinjury activities. It has been suggested providing rehabilitation training to resolve the limited knee range of motion and quadriceps strength deficit is advantageous toward the functional performance prior to and after the reconstruction surgery^{31,32}. The pre-surgical quadriceps strength status was found to predict patient-reported knee function measures after surgery^{33,34}. De Jong and colleagues reported that the pre-surgical quadriceps strength is associated with single hop test performance 9 months after surgery²³. Therefore, the overall goal of the rehabilitation programs after ACL rupture is to resolve patients' impairments and functional limitations.

In addition to the knee impairments and functional limitations, majority of patients with ACL rupture adapt a remarkable abnormal gait pattern and maladaptive neuromuscular changes during different functional activities (i.e. walking, jogging, and running)^{6,12,35,36}. This abnormal gait pattern is characterized by reduced knee joint

motion and external knee moment, shifted knee moment support away from the knee joint, and generalized co-contraction of the muscles that cross the knee joint^{6,35,37}. The magnitudes of gait abnormalities become more pronounced during high physical activities³⁵. It was reported that quadriceps strength deficit contribute to the abnormal knee kinematics and kinetics³⁸. Roewer and colleagues, however, reported that involved limb gait abnormalities continue to exist despite adequate quadriceps strength¹⁴.

The combination of functional limitation and abnormal gait pattern are contributing factors for patient's functional performance and for knee joint health and integrity. Long-standing functional limitation and abnormal gait pattern may have serious implications for subsequent injury and may lead to the development of knee osteoarthritis^{23,39,40,41}. Andriacchi and colleagues reported early reduction in cartilage thickness was caused by abnormal gait motion and cartilage thinning was common in the region that was unloaded after ACL rupture⁴². A recent study identified underlying kinematics and kinetics abnormalities during drop vertical jump as predictive of second ACL injury after reconstruction surgery⁴³.

For patients who are considering reconstruction surgery, resolving knee impairment, functional limitations, and restoring normal motion before surgery is a key factor for optimizing the functional recovery and improving the functional outcomes after reconstruction surgery. Therefore, it is important to provide appropriate and progressive intervention training to resolve knee impairments, functional limitations, and abnormal gait pattern. Further, it is important to integrate neuromuscular training to restore the maladaptive neuromuscular changes and neuromuscular deficits after

ACL rupture to enhance patients' functional performance and to heighten the possibility for patient to return to their activities with minimum to no limitation.

1.2 Altered Muscle Activation Pattern: Magnitude and Timing

Dynamic knee instability or “episodes of knee giving way” is a common symptom of ACL rupture during functional activities. These episodes of knee instability may indicate muscles weakness and neuromuscular dysfunction to adequately stabilize the knee joint. The repeated occurrence of dynamic knee instability is problematic to the joint integrity as it may cause traumatic injuries to the menisci and articular cartilage of the knee joint^{16,28,44}. Patients attempt to compensate for the recurrence of dynamic knee instability by limiting the knee joint motion and adapting gross muscular co-contraction to protect the knee joint. The neuromuscular system compensates to dynamic knee instability through gross muscular co-contraction and altered timing and duration of muscle activates to stabilize the knee joint; especially hamstring and gastrocnemius muscles^{12,45,46}. Muscle co-contraction is defined as a simultaneous activation of the agonist-antagonist muscles that cross the knee joint. Rudolph and colleagues reported changes to the activation of knee flexor muscles (hamstring and gastrocnemius) include increasing the magnitude of muscle activities and time duration of muscle activity during the stance phase of gait¹². The increase in muscle activation of the knee flexor muscle simultaneously increases the knee joint stiffness. The underlining changes that coincide with muscle co-contraction include early onset, longer total duration, longer duration from onset-to-peak, or delayed termination and a delayed peak activity of the knee flexor muscles activities^{12,47}. It has been reported that most of patients with ACL rupture demonstrated delayed peak muscle activity and longer duration between onset-to-peak muscle activities for knee flexor muscle^{12,48}.

These delays indicate that knee flexor muscle are not generating enough force in an appropriate time to control the external moments applied on the knee joint during walking. This in turn may cause knee giving ways during dynamic functional activities. Beard and colleagues reported a relationship between delayed knee hamstring muscle activities in patients with ACL rupture and the episodes of knee giving ways⁴⁸. The association between the magnitude of knee flexor muscle co-contraction and the duration of onset-to-peak muscle activation, however, has not been defined.

Though muscular co-contraction has been advocated as a response that protects the knee joint, it has the potential to harm the knee joint. Muscular co-contraction may increase compressive forces and alter the joint loading of the knee joint that may initiate the processes of knee osteoarthritis^{49,50}. Resolving the abnormal muscular co-contraction of the knee flexor and extensor muscle may be beneficial for the health of knee joint and for the performance of the patients during participation in highly physical activities. Resolving muscle co-contraction may reduce the compressive joint forces and restore the normal loading mechanism and normal joint motion.

Administration of neuromuscular re-education training normalizes knee movement pattern and reduces muscular co-contraction^{36,51}. Manual perturbation training is a form of neuromuscular training that has a positive effect on the neuromuscular system. Manual perturbation training has been shown to improve muscular co-contraction strategies and promote selective muscle activation patterns in patient with ACL rupture^{36,51}. It is unknown; however, whether administering perturbation training using a mechanical device provides effects similar to manual perturbation on the muscle co-contraction and on the timing duration of onset-to-peak

muscle activity of patients with ACL rupture. It is also unknown whether the time duration from onset-to-peak muscle activity of the thigh and leg muscles are associated with the muscular co-contraction, and whether the changes in the time from onset-to-peak muscle activity induced by perturbation training associate with changes in the magnitude of the muscle co-contraction. Understanding the relationship between the timing duration of onset-to-peak muscles activity and the muscular co-contraction might allow clinicians to modify the ACL rehabilitation programs to restore the normal muscle activity pattern and normal gait motion, and reduce the compressive forces between joint's articular surfaces.

1.3 Neuromuscular Training: Manual and Mechanical Perturbation

Early after ACL rupture, the rehabilitation program focuses on treating knee impairments related to joint effusion, range of motion deficits, and quadriceps weakness. Resolving knee impairments is a key for knee function recovery; however, it is insufficient for patients who plan to participate in high physical activities. The effective rehabilitation training should take the gait abnormalities, limb-to-limb movement asymmetry, and maladaptive neuromuscular strategies into consideration to allow patients to return safely and successfully to high physical activities.

The current clinical practice guidelines for patients with knee ligament sprains suggests administration of progressive quadriceps strength training augmented with neuromuscular training, specifically manual perturbation training, to facilitate returning to preinjury activities^{52,53}. Manual perturbation training includes administration of purposeful manipulation of support surfaces (i.e. rockerboard, rollerboard, and rollerboard and platform) by a physical therapist⁵. The manual perturbation training is an effective intervention that promotes dynamic knee stability,

abates abnormal gait pattern, improves knee functional performance, reduces muscle co-contraction, and promotes selective muscle activation strategies^{5,15,36}. The perturbation training, however, is not widely used as part of the ACL rehabilitation program in the United States due to lack of equipment. Furthermore, the perturbation training is administered manually which requires extensive physical labor and an extensive one-on-one time from the treating therapist⁵⁴. The effect of administering perturbation training using mechanical device similar to the manual training as part of the ACL rehabilitation program may help resolving these issues.

Using a mechanical device that provides perturbation training similar to the manual perturbation training may facilitate the use of the training in a wide range of the rehabilitation clinics. Additionally, this allows administering controlled and standardized perturbation stimuli throughout the rehabilitation clinics with an attempt to standardize the ACL rehabilitation programs. Mechanical perturbation devices have been used in rehabilitation clinics as interventions that re-educates the proprioceptive system, improves mechanoreceptor function, and restores normal neuromuscular coordination by exposing the patients to a controlled and progressive preprogramed translation of support surfaces in different directions⁵⁵⁻⁵⁷. Furthermore, mechanical perturbation has the potential to improve balance abilities⁵⁵, increase postural reflex by reducing reaction time⁵⁸, improve balance and stability in patients with OA⁵⁹, and enhance the timing and pattern of muscle activation⁶⁰.

Simbex LLC has developed a prototype, automated mechanical perturbation device, “Reactive Agility System”. The Reactive Agility System provides mechanical perturbations based on controls and settings that were set by the physical therapist. The device has a moveable plate that provides standardized multidirectional

translations including rotation in the horizontal plane (three degrees of freedom (3DOF)) similar to the manual perturbation training. The results of this study will investigate whether incorporation of a mechanical perturbation device into the ACL rehabilitation program will be beneficial to improve dynamic knee stability and knee function and restore normal knee biomechanics, limb movement symmetry, and returning to preinjury activity. Furthermore, it will help to evaluate whether mechanical perturbation can provide an effect similar to manual training, so mechanical perturbation may replace manual perturbation training and reduces the extensive physical labor and the amount of time a therapist needs to treat a single patient in a clinical rehabilitation setting. The proposed automated platform device may translate into commercially viable, cost-effective, controllable, and clinically relevant testing device that can also be used in clinical and research settings.

1.4 Poor Outcomes after ACLR

Most of athletes choose to undergo early ACL reconstruction (ACLR) to prevent further damage to the knee structures, to restore mechanical knee stability, and to expedite the process of returning to the preinjury activity level^{28,61,62}. The first year after ACLR, however, is a highly vulnerable time for patients attempting to return to preinjury activities as surgery related impairments, poor knee functional performance, quadriceps strength deficit, limb-to-limb movement asymmetries, and neuromuscular dysfunction continue to persist after ACLR⁶³. While ACLR restores mechanical knee stability, the outcomes after surgery are poor and variable as not all athletes can return to their preinjury activity level or restore full knee function. The poor outcome measures after ACLR surgery may associate with factors related to the knee functional

limitations and biomechanical maladaptive and with the criteria that are used to clear patients to return to the preinjury activity level.

The current outcome measures that are used to evaluate the success after ACLR includes returning to the preinjury activity level and minimizing the risk for secondary ACL injury or further knee injuries⁶⁴. The post-surgical rehabilitation program targets resolution of the knee impairment and functional deficits⁶⁵. Patients receive a progressive rehabilitation program with the attempt to achieve normal limb movement symmetry, adequate quadriceps strength and running with no adverse response⁶⁵. However, a group of patients continue to exhibit quadriceps strength deficit, limb-to-limb asymmetry, and score low on patient-reported measures^{14,23,25,66,67}. These functional limitations and limb-to-limb movement asymmetry might be contributing factors to the poor outcomes after ACLR.

The rate of return to preinjury activity level at different time points after ACLR was 55%⁶⁸, however, only 33% of athletes returned to full competition in sport activities one year after ACLR⁶⁹. Additionally the risk for second ACL injury is high after ACLT. Patients with ACLR are 15 times more likely to sustain another ACL rupture compared to healthy individuals⁷⁰. Additionally, patients with ACLR who returned to participate in the preinjury activity level possess up to 30% risk for secondary ACL rupture during the first year after ACLR⁷¹. Furthermore, up to 21% of athletes who returned to their sports had major functional limitations that could lead to reduced level of performance⁷². The poor outcomes following ACLR surgery highlight the concerns over the criteria that are used to define readiness to return to preinjury activity level. It is important for clinicians to utilizing a comprehensive set of objective criteria to accurately determine patients' readiness to return to preinjury

activity levels. Further, it is important to identify those patients with functional limitations and limb-to-limb asymmetry prior to clear them to return to their preinjury activity to avoid secondary ACL injury or further damages to the knee joint.

1.5 Return to Activity Criteria

The current rehabilitation programs after ACLR focus on early knee mobilization, resolving knee impairments, and weight-bearing strength training to yield good outcomes including normal knee function and returning to the preinjury activity level⁶⁵. The progression throughout the rehabilitation program is guided by achieving specific milestones to achieve successful outcomes after ACLR⁶⁵. Each patient responds to the rehabilitation training differently as some patients might improve their knee functionality faster than others whom may require an extended training program to achieve their rehabilitation program's milestone. Therefore, it is important to evaluate each patient individually using objective criteria to assure that the patients are adequately prepared to be progressed to the next level of rehabilitation training. Additionally, it is important to evaluate patients' readiness to be discharged from the rehabilitation program or to be cleared to return to the preinjury activity level using a set of objective criteria instead of solely time from surgery. Further, it is important to use a comprehensive set of functional tests that can capture functional deficits and reflect the functional performance level of the patients so clinicians can use as criteria to clear patients to return to preinjury activity level.

One challenge after post-surgical rehabilitation is determining patients' readiness to return to a preinjury activity level. Many patients are cleared to return to their preinjury activity level based on the time from surgery (typically 6 months after ACLR)^{61,73}. While time from surgery approach takes the graft healing processes into

account, patient's knee impairments, functional performance, or limb-to-limb movement asymmetry may not have resolved. Therefore, clearing patients having unresolved impairments and poor functional performance into high demand physical activities solely based upon the time approach may have a negative influence on outcomes and predispose patients for further knee injuries after ACLR.

Currently, there is no consensus regarding what constitutes "satisfactory" return to activity criteria after ACLR. Criteria related to the achievement of mechanical knee stability, minimum quadriceps strength deficits, and the time from surgery are frequently used as guidelines to clear patients to return to their preinjury activity levels^{74,75}. Barber-Westin et al reported that only 15% of studies report using the time from surgery along with subjective factors to determine return to unrestricted sports activities after ACLR and that only 13% of studies report using objective criteria such as lower extremity muscle strength, limb movement symmetry, knee range of motion, and joint effusion⁷⁶.

Our research group quantitatively determines clearance to return to activities using strict return to activity criteria (RTAC) that emphasizes good knee function and normal limb-to-limb symmetry. The RTAC consists of a battery of performance-based tests including quadriceps strength and four single-legged hop tests (single hop, cross-over hop, triple hop, and 6-meter timed hop) and two patient-report questionnaires (Knee Outcome Survey-Activities of Daily Living Scale and Global Rating Score of perceived knee function). Quadriceps strength and single-legged hop performance are sensitive to changes over time, which may reveal meaningful improvements and provide clinical information regarding functional recovery after ACLR^{77,78}. Additionally, patients with minimum quadriceps strength deficit demonstrate

functional performance similar to healthy individuals⁷⁹. These RTAC are comprehensive as they encompass both functional performance tests and patient-reported measures. Performance –based tests replicate the demands of on field performance of sport activities including jumping, cutting, pivoting, taking-off, and landing maneuvers^{80,81}. Additionally, these criteria ensure that athletes are fully rehabilitated and their knees are ready to meet the demands of their sport. Logerstedt and colleagues reported that performance-based measures including the single-legged hop tests 6-months after ACLR are determinants for normal and poor knee function one year after ACLR⁸⁰. Using a battery of RTAC that include performance-based tests and patient-reported measures in rehabilitation clinic may allow clinicians to identify patients with poor knee function and limb movement asymmetry early after ACLR or after an extended period of time after ACLR. Additionally, RTAC may allow clinicians to identify patients who are at a high risk for secondary knee injury early after surgery and who are most likely will not return to participate in the same preinjury activity level after ACLR. Therefore, implementing RTAC in rehabilitation clinics will allow clinicians also to identify patients with abnormal knee function and limb-to-limb asymmetry that require additional training to address functional deficits and movement asymmetry before allowing these patients to return to their preinjury activities.

1.6 Predict Return to Participate in the Same Preinjury Activity Level after ACLR

Returning to participate in sport activities is a desire for most individuals after ACLR. There are multiple factors that have been advocated to be associated with the return to the preinjury sport activities. Only explanatory variables, however,

related to patients' demographics, concomitant injuries, and treatment variables that are associated with returning to preinjury activity levels after ACLR have been investigated⁸²⁻⁸⁴. Some investigators used functional performance variables to predict patient-reported outcomes. Logerstedt and colleagues reported that performance-based variables including single-legged hop tests are determinants for normal and poor knee function one year after surgery⁸⁰. Dunn and colleagues reported that a higher preinjury activity level and lower body mass index were associated with the higher activity level at two years after ACLR, while female sex, those who were smoking during the 6 months before the ACLR, and revisions ACLR were associated with a lower activity level⁸⁵. Ardern and colleagues reported that younger men individuals who played elite sport and having a positive psychological response were factors that favored returning to the preinjury sport level²⁵. It is unknown, however, whether variables related to patient functional performance and patient-reported measures can predict returning to participate in the same preinjury activity level after ACLR.

Our RTAC variables were constituted to ensure normal knee function and limb-to-limb movement symmetry to meet the demands of high physical activities. Additionally, RTAC variables can replicate the demands resemble to on-field performance of sport activities that include jumping, cutting, pivoting, taking-off and landing of hop task. A recent systemic review and meta-analysis study reports that return to preinjury activity level was favored in athletes with symmetrical hopping performance and in athletes who participate in running, pivoting, decelerating, and pivoting activities⁶⁸. Additionally, previous work used similar variables to the RTAC reported that these variables can distinguish between those patients with dynamic knee stability from those patients with knee dynamic instability early after ACL injury^{86,87}.

Additionally, these same variables can predict who can successfully return to participate in the same preinjury activity level in the short term in patients who were treated non-surgically⁸⁷. Therefore, utilizing a battery of performance-based tests and patient-reported measures in rehabilitation clinics may be determinants for return to preinjury activity level after ACLR. Furthermore, RTAC have been instituted to determine patients' readiness to return to preinjury activities after ACLR, therefore, these RTAC variables may contribute to the ability of predicting return to participate in the same preinjury activity level at midterm and long term after ACLR.

1.7 Aims and Hypothesis

The goals of this study were firstly to examine the knee functional performance and patient-reported measures at 12 months (12-M) and 24 months (24-M) after ACLR between those subjects who demonstrate normal knee function and limb-to-limb movement symmetry (PASS RTAC) and those with poor knee function and limb-to-limb movement asymmetry (FAIL RTAC) at 6 months (6-M) after ACLR and how their functional performance changes over time. Additionally, this work will investigate whether administering 10-training session of mechanical perturbation training using the 3DOF plate provides effects similar to 10-training sessions of manual perturbation training on knee mechanics, knee functional performance, and neuromuscular compensations in patients with an acute ACL rupture who are managed non-surgically.

Aim 1. To investigate the functional performance-base and patient-reported measures at 12-M and 24-M after ACLR between those patients who passed (PASS) and those who failed (FAIL) on RTAC 6-M after ACLR and how their functional performance changes over time.

- Hypothesis 1.1 Subjects who PASS RTAC at 6-M after ACLR will PASS RTAC at 12-M and 24-M after ACLR, while subjects who FAIL on RTAC at 6-M after ACLR will continue to FAIL RTAC by demonstrating poor knee function performance and limb-to-limb movement asymmetry at 12-M and 24-M after ACLR.
- Hypothesis 1.2 The FAIL group will demonstrate greater improvements in performance-based measures compared to the PASS group between the period of 6-M to 12-M and 12-M to 24-M after ACLR with the greatest improvement occurring during the first year after ACLR.
- Hypothesis 1.3 FAIL group will demonstrate greater improvements in patient-reported measures compared to the PASS group between the period of 6-M to 12-M and 12-M to 24-M after ACLR with the greatest improvement occurring during the first year after ACLR. **Aim 2.** To investigate whether RTAC variables at 6-M after ACLR predict return to participate in the same preinjury activity level 12-M and 24-M after ACLR and to investigate which combination of RTAC variables 6-M after ACLR predicts return to participate in the same preinjury activity levels 12-M and 24-M after ACLR.
- Hypothesis 2.1 Subjects who PASS RTAC at 6-M after ACLR are more likely will return to the same preinjury activity level at 12-M and 24-M after ACLR while subjects who FAIL RTAC at 6-M after ACLR are more likely will not return to the same preinjury activity level at 12-M and 24-M after ACLR.

- Hypothesis 2.2 RTAC variables will predict return to participate in the same preinjury activity level at 12-M and 24-M after ACLR.
- Hypothesis 2.3 A combination of functional performance and patient-reported measures will explain a large portion of variance of return to participate in the same preinjury activity level at 12-M after ACLR.
- Hypothesis 2.1 A combination of functional performance measures will explain a larger portion of the variance of return to participate in the same preinjury activity level 24-M after ACLR.

Aim 3. To evaluate whether administration of 10-training sessions of mechanical perturbation using 3DOF plate provides similar effect as using the manual perturbation training on gait mechanics, functional performance-based, and patient-reported measures in athletes with ACL rupture.

- Hypothesis 3.1 Subjects who receive 10-training sessions of mechanical perturbation training using the 3DOF plate will demonstrate knee kinematics similar to those subjects who receive 10-training sessions of manual perturbation training at post-training testing session.
- Hypothesis 3.2 Subjects who receive 10-training sessions of mechanical perturbation training using the 3DOF plate will demonstrate knee kinetic similar to those subjects who receive 10-training sessions of manual perturbation training.
- Hypothesis 3.3 Subjects who are trained on the 3DOF plate will be equally likely to PASS RTAC compared to subjects who are trained on the manual perturbation training.

- Hypothesis 3.4 Subjects who are trained on the 3DOF plate will improve their performance-based and patient-reported measures similar to those subjects who are trained on the manual perturbation training.

Aim 4. To investigate whether administration of 10-training sessions of mechanical perturbation using the 3DOF plate provides similar effects as 10-training sessions of manual perturbation training on muscle activation time and muscle co-contraction measures in athletes with ACL rupture.

- Hypothesis 4.1 Subjects who are trained on the mechanical perturbation device using the 3DOF plate will demonstrate a reduction in muscle co-contraction indexes on the involved limb, similar to subjects who are trained on the manual perturbation training at post-training testing session compared to pre-training testing.
- Hypothesis 4.2 Subjects who are trained on the mechanical perturbation training using the 3DOF will demonstrate short duration of onset time-to-peak muscle activity for hamstring, gastrocnemius, and soleus muscles similar to those who are trained on the manual perturbation training at post-training testing session compared to the pre-training testing.
- Hypothesis 4.3 The length of onset time-to-peak muscle activity will positively correlate with the muscle co-contraction indexes at post-training testing session and pre to post-training change in onset time-to-peak muscle activity will correlate with the muscle co-contraction of the hamstring, gastrocnemius, and soleus muscles at post-training testing session in manual and 3DOF groups.

Chapter 2

SUBJECTS WHO FAIL RETURN TO ACTIVITY CRITERIA SIX MONTHS AFTER ACL RECONSTRUCTION CONTINUE TO DEMONSTRATE DEFICITS AT TWO YEARS

2.1 Abstract

Background: The variability in the outcomes after anterior cruciate ligament (ACL) reconstruction (ACLR) might be associated with clearing athletes with functional limitations and limb-to-limb movement asymmetry to return to high demand physical activities. A battery of return-to-activities criteria (RTAC) that emphasizes good knee function and normal limb-to-limb symmetry has been instituted to quantitatively determine athletes' readiness to return to activities. The purpose of this study was to investigate performance-based and patient-reported measures 12 months (12-M) and 24 months (24-M) after ACLR surgery between subjects who PASS (scored $\geq 90\%$) or FAIL (scored $< 90\%$) on RTAC at 6 months (6-M) after ACLR; and to further investigate how their functional performance and patient-reported measures change over time.

Methods: One hundred and eight level I or II subjects with ACLR included in this study. After ACLR, subjects completed a battery of return to activity criteria (RTAC) testing at 6-M, 12-M, and 24-M follow up testing. RTAC included performance-based tests ((isometric quadriceps strength and four single-legged hop tests: single hop, cross-over hop, triple hop, and 6-meter timed hop) and two patient-reported questionnaires (Knee Outcome Survey-Activities of Daily Living Scale and the Global Rating Score of perceived knee function) at 6-M, 12-M, and 24-M after ACLR. Limb symmetry index (LSI) for quadriceps index (QI) and single-legged hop tests was calculated as the ratio of the performance of the involved limb to uninvolved

limb x 100. Subjects who scored $\geq 90\%$ on all RTAC were classified as PASS group and those who scored $< 90\%$ on any of RTAC were classified as FAIL group.

Result: Ninety-five subjects completed the followed up testing at 6-M after ACLR, 48 subjects (50.5%) PASS RTAC and 47 subjects (49.5%) FAIL. At 12-M after ACLR 80 subjects completed the followed up testing, 31 subjects f PASS and 15 subjects from those who FAIL on RTAC at 6-M after ACLR passed the criteria again at 12-M after ACLR. In comparison 23 subjects who FAIL and 11 subjects form those who PASS RTAC at 6-M after ACLR failed again on the criteria at 12-M after ACLR. At 24-M after ACLR 60 subjects completed followed up testing, 25 subjects who PASS and 14 from those who FAIL on RTAC at 6-M after ACLR passed the criteria again at 24-M after ACLR. While 13 subjects who FAIL and 8 subjects from those who PASS RTAC failed again on the criteria 24-M after ACLR. A significant group by time interaction was found for single hop ($P=0.006$) and 6-meter timed hop LSIs ($p=0.037$). A significant main effect of group was detected for quadriceps index, cross-over hop, and triple hop LSIs ($p<0.01$). Main effect of time was detected for cross-over hop and triple hop LSIs, and GRS ($p<0.05$).

Discussion: Subjects who Passed RTAC early after ACLR are more likely to demonstrate normal knee function and limb-to-limb movement symmetry at 12-M and 24-M after surgery. While those subjects who failed on RTAC early after ACLR are more likely to demonstrate impaired knee function and limb-to-limb movement asymmetry at 12-M and 24-M after surgery. FAIL group demonstrated greater improvement on performance-based measures compared that was achieved between 6-M and 12-M after ACLR.

2.2 Introduction

The anterior cruciate ligament (ACL) is the most commonly injured ligament in the knee joint among young individuals who participate in jumping, cutting, and pivoting activities^{69,88}. ACL rupture results in a variety of structural and functional impairments that challenges patients' ability to perform both daily living and sports activities⁸⁹. Currently, ACL reconstruction (ACLR) surgery has been advocated as the standard of care for active individuals desiring to return to high-level activities after ACL rupture⁶². The common goal of ACLR is to restore mechanical knee stability, normal knee function, and limb movement symmetry in order to prevent damages to the knee structures and to facilitate a return to multidirectional sport activities^{28,62,90,91}. In the United States approximately 125,000 ACLR surgeries are performed annually⁹². Although ACLR has been shown to restore knee mechanical stability^{93,94}, quadriceps strength deficits, poor knee functional performance, limb-to-limb movement asymmetries, and neuromuscular dysfunction often continue to persist long after ACLR^{19,23-27}. Additionally, the rate of return to preinjury activity levels is lower than anticipated and the incidence of secondary ACL injury is high⁶⁸.

One challenge of post-surgical rehabilitation is determining a patient's readiness to return to a preinjury activity level. Many patients are cleared to return to their preinjury activity level based on the time from surgery (typically 6 months after ACLR)^{61,73}. While time from surgery approach takes the graft healing processes into account, a patient's knee impairments, functional performance, or limb-to-limb movement asymmetry may not have resolved. Therefore, clearing patients having unresolved impairments and functional performance into high demand physical activities solely based upon the time approach may have a negative influence on outcomes after ACLR and predispose patients for further knee injuries.

A successful return to preinjury activity level and a low incidence of secondary knee injury after ACLR are desired outcomes; however such outcomes tend to be less than optimal^{24,71}. Ardern et al reported that 55% of athletes returned to competitive level sport after surgery⁶⁸, however only one-third of the athletes attempted full competition in sports activity at one year after ACLR⁶⁹. Athletes after ACLR are 15 times more likely to experience secondary ACL injury compared to healthy individuals⁹⁵. In addition, athletes who did return to preinjury activity level displayed a risk for secondary ACL injury as high as 30% within the first year after ACLR¹⁹. Furthermore, up to 21% of athletes who returned to their sports had major functional limitations that could lead to reduced level of performance⁷². The poor outcomes following ACLR surgery highlight the concerns over the criteria used to define readiness to return to preinjury activity level, and further point to the absence of a consensual, comprehensive set of objective criteria to be used accurately to determine patients' readiness to return to preinjury activity levels.

Currently, there is no consensus regarding what constitutes "satisfactory" return to activity criteria after ACLR. Criteria related to the achievement of mechanical knee stability, minimum quadriceps strength deficits, and the time from surgery are frequently used as guidelines to clear patients to return to their preinjury activity levels^{74,75}. Barber-Westin et al reported that only 15% of studies report using the time from surgery along with subjective factors to determine return to unrestricted sports activities after ACLR and that only 13% of studies report using objective criteria such as lower extremity muscle strength, limb movement symmetry, knee range of motion, and joint effusion⁷⁶. Recently, comprehensive return-to-activities criteria (RTAC) that include both performance-based and patient-reported measures

have been used to determine patient's readiness to return to multidirectional activities^{22,87,96}. Using strict RTAC that emphasizes good knee function and normal limb-to-limb symmetry can quantitatively determine clearance to return to activities. This RTAC consist of a battery of performance-based tests including quadriceps strength testing, four single-legged hop tests (single hop, cross-over hop and triple hop for distance, and 6-meter timed hop), and two patient-report questionnaires (Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS) and Global Rating Score of perceived knee function (GRS)). The majority of these RTAC variables are sensitive to knee functional changes over time and have the potential to provide therapists with clinically relevant information, including patients' responses to different therapeutic interventions^{25,96}. Additionally, RTAC have been instituted to ensure that patients are fully rehabilitated by demonstrating normal knee function and limb-to-limb movement symmetry to allow them to meet the demands of their sports activity. However, it is unknown whether patients demonstrating poor knee functional performance and limb-movement asymmetry on RTAC early after ACLR will continue to fail on RTAC after an extended period of time. Consequently, the purpose of our study was to investigate both functional performance and patient-reported measures at 12 months (12-M) and 24 months (24-M) after ACLR between those subjects who PASS (scored > 90%) and those who FAIL (scored < 90%) on RTAC at 6 months (6-M) after ACLR, and to further investigate how their functional performance and patient-reported measures change over time.

2.3 Methods

One-hundred and eight subjects with an ACLR were pulled out from an ongoing, prospective cohort study. These subjects had a complete unilateral ACL

injury. All subjects were regular participants in level I or II activities⁷ including jumping, cutting, pivoting, and lateral movements for more than 50 hours/year prior to their injury. Excluded from the study were subjects having concomitant ligamentous injury, repairable meniscal injury, full-thickness articular cartilage damage, or a history of serious ipsilateral or contralateral lower extremity injury (i.e., fracture). Sixty-eight (63.2%) of subjects received 10-sessions while the rest received at least 4-sessions of pre-operative rehabilitation training that included progressive quadriceps strengthening and specific perturbation training as described by Fitzgerald et al^{5,97}. Ligament reconstructions were performed for 108 subjects using a soft tissue allograft (n=69), a semitendinosus-gracilis autograft (n=37), or a bone patellar tendon-bone autograft (n=2).

After surgery, all subjects underwent a supervised, progressive post-surgical rehabilitation protocol that targets early resolution of joint effusion, range of motion deficits, quadriceps strength impairments, and functional limitations that included early weight-bearing⁶⁵. Functional data were collected from subjects at 6-M, 12-M, and 24-M after ACLR. The study was approved by the University of Delaware Institutional Human Subjects Review Board. Subject recruitment was done through the University of Delaware Physical Therapy Clinic. All subjects provided written informed consent for participation in this study.

Although one-hundred and eight subjects were enrolled in the study, complete functional and patient-reported data were only available for 95 subjects (Men: 63; Women: 32; mean age: 27.14 ± 10.59) at 6-M (mean: 6.26 ± 0.81 months), 80 subjects (Men: 51; Women: 29) at 12-M (mean: 12.44 ± 1.13 months), and for 60 subjects (Men: 38; Women: 22) at 24-M (mean: 25.1 ± 4.16 months) follow up testing sessions

after ACLR. Data were unavailable for 13 subjects at 6-M, 15 subjects at 12-M, and for 20 subjects at 24-M after ACLR for a variety of reasons (Figure 1).

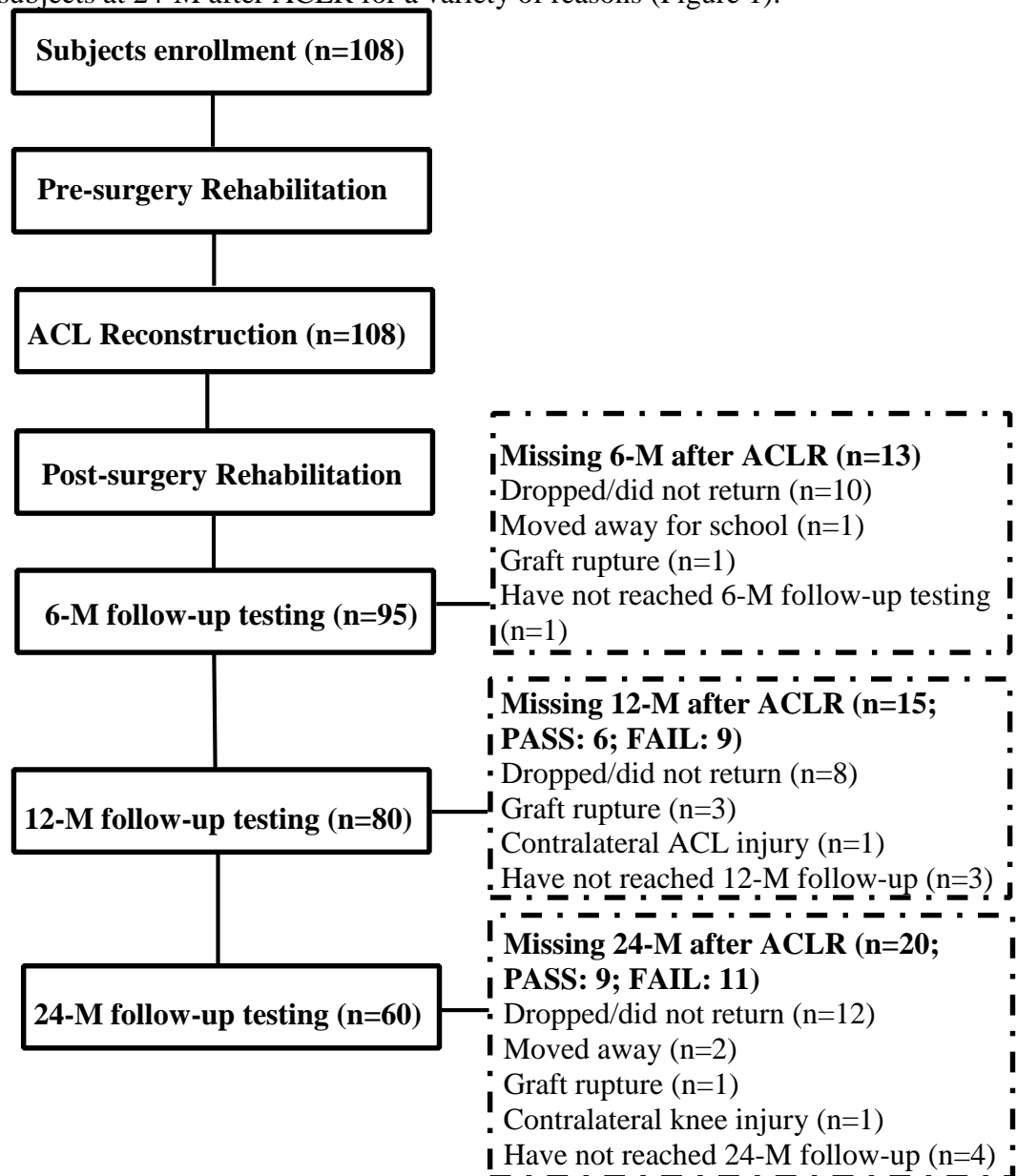


Figure 1 Flow diagram for subjects' participation at 6-m, 12-m and 24-m follow-up testing after ACLR

2.4 Testing

Subjects completed a battery of performance-based tests including quadriceps strength testing and four single-legged hop tests and two patient-reported questionnaires of knee function including KOS-ADLS and GRS at 6-M, 12-M and 24-M after ACLR^{24,25}.

2.4.1 Performance-Based Measures

Quadriceps strength was measured using a maximal voluntary isometric contraction (MVIC) of the quadriceps muscle on an electromechanical dynamometer⁹⁸ (Kin-Com, Chattanooga Corp, Chattanooga, TN). Subjects were seated with hip and knee flexed to 90° with stabilization at the hip, knee, and ankle (Figure 2). Subjects performed three practice trials before testing (two sub-maximal and one maximal effort). Upon testing, subjects were instructed to maximally contract their quadriceps muscle. Testing was first completed on the uninvolved limb followed by the involved limb with no more than three quadriceps strength tests being performed on any limb to avoid muscle fatigue. Quadriceps index (QI) was calculated by dividing the involved quadriceps muscle force by the uninvolved quadriceps muscle force, multiplied by 100. At 6-M follow-up testing, one subject did not complete quadriceps strength testing as a result of patellofemoral pain. At 24-M follow-up testing, another subject did not complete quadriceps strength testing because of a recent ankle fracture.

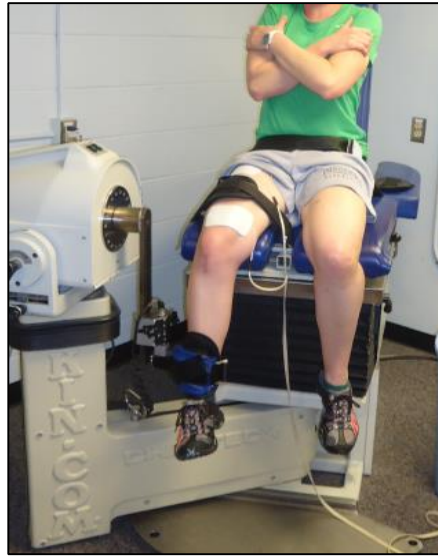


Figure 2 Maximal voluntary isometric contraction (MVIC).

Hop performance testing was measured using a series of single-legged hop tests⁹⁹: single hop for distance, cross-over hop for distance, triple hop for distance, and 6-meter timed hop (Figure 3). Subjects were required to demonstrate symmetrical knee range of motion, minimal knee joint effusion¹⁰⁰, QI greater than or equal to 80%, and be pain-free while hopping up and down on the involved limb prior to the hopping tests. All hop-test data collected at 6-M and 12-M included in this study were collected from subjects wearing a functional knee brace, while 24-M hop data was collected without a brace. All subjects performed two practice trials followed by two measurement trials of each hop test on both limbs. Measurement trial results were counted if subjects maintained balance during landing without touching the ground with the uninvolved foot. Hop performance limb symmetry indexes (LSIs) were calculated as the percentage of the averaged involved limb hop distances divided by

the averaged uninvolved limb hop distances for each individual distance hop test, multiplied by 100. The 6-meter timed hop was calculated by dividing the percentage of the averaged uninvolved limb hop time divided by the averaged involved limb hop time, multiplied by 100. At 6-M follow-up testing, five subjects did not complete single-legged hop tests (one subject demonstrating increased knee joint effusion, two subjects demonstrating QI < 80%, one subject reporting patellofemoral pain, and one subject reporting foot pain and knee joint effusion). At 12-M follow-up testing, four subjects did not complete the hop tests (two subjects demonstrating QI < 80%, one subject experiencing lower extremity pain during the hop test, and one subject reporting fear of experiencing knee instability during the hop test). At 24-M follow-up testing, seven subjects did not complete the hop tests (one subject demonstrating QI < 80%, one subject reporting chronic bilateral plantar fasciitis, one subject reporting medial knee pain, one subject demonstrating knee joint effusion, one subject refusing to hop from fear of experiencing knee instability, one subject having a recent ankle fracture, and one subject having a graft rupture).

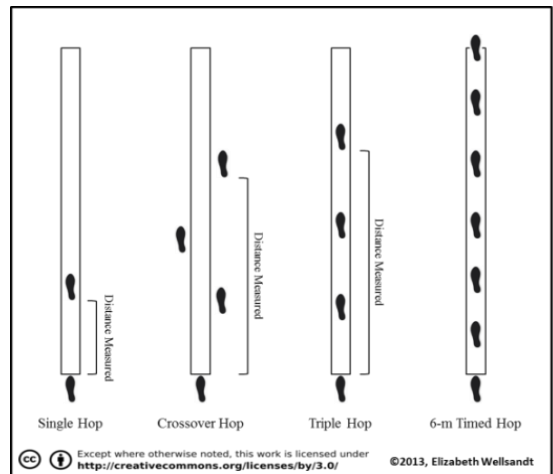


Figure 3 Four single-legged hop tests

2.4.2 Patient-Reported Measures

Following all performance-based testing, subjects filled out patient-reported questionnaires: KOS-ADLS and GRS to allow subjects to better rate their knee functional status. The KOS-ADLS, a 14-item, patient-reported questionnaire consists of the subjects' perception of their knee symptoms and functional limitations related to ACLR and how these limitations affect their ability to perform activities of daily living such as walking, ascending and descending stairs, kneeling, sitting, and squatting¹⁰¹. The KOS-ADLS has been shown to be a reliable, valid, and responsive measure for assessing knee functional limitations with high intraclass coefficients of 0.97 with test-retest reliability¹⁰². KOS-ADLS scores are reported as a percentage of the subject's points divided by the total possible points, multiplied by 100. The GRS, used to assess subjects' current knee functional performance, is a one-item question that asks subjects to rate their current knee function on a scale from 0% to 100%, with 0% being the inability to perform any activity and 100% being their level of knee function prior to injury, including sports activities. It has been reported that analogue GRS has a high test-retest intraclass coefficients of 0.96¹⁰³.

2.5 Return to Activity Criteria

All subjects were cleared to begin gradual reintegration into their preinjury activity once they achieved at least 90% on all performance-based and patient-reported measures. Subjects who achieved scores of 90% or more on all RTAC at 6-M were categorized as PASS group and those who failed to achieve 90% on any of RTAC were categorized as FAIL group. These criteria were only used to classify subjects as PASS or FAIL at 6-M after surgery.

2.6 Statistical Analysis

Independent t-test was used to determine differences between groups for subjects' demographics and to compare mean differences of RTAC variables between PASS and FAIL groups at 6-M after ACLR. Chi square test was used to determine significant differences between groups in women to men ratio. In case chi square test is significant, independent t-test was used to evaluate whether significant difference existed between women to men in each group or between women to men in overall. Likelihood ratios (LHR) were used to determine the relationship between subjects who FAIL on RTAC at 6-M and those subjects who continued to FAIL on RTAC at 12-M and 24-M after ACLR. A 2 x 3 repeated measures analysis of variance was used to determine the relationship between the groups (PASS or FAIL) and over time (6-M, 12-M, and 24-M) for each RTAC. Bonferroni corrections were used to adjust for multiple comparisons. Univariate analysis of variance was used to determine whether PASS and FAIL groups demonstrated significant improvement between various follow-up time points. All data were analyzed with SPSS 20.0 (IBM Company, Chicago, Illinois) with a significance level of 0.05 set a priori.

2.7 Results

Ninety-five subjects completed 6-M, 80 subjects completed 12-M, and 60 subjects completed 24-M follow-up testing after ACLR (Figure 1). Six months after ACLR, 48 subjects (50.5%) PASS RTAC (pass time avg: 6.41+2.69 months) and 47 subjects (49.5%) FAIL on RTAC. At 6-M after ACLR, there was no difference in age and BMI between PASS and FAIL groups ($p>0.05$), however, the percentage of women to men was significantly different between groups with more men in the PASS group than women ($P= 0.03$). Post hoc test shown that the number of men subjects

was significantly higher than the number of women subjects in the study overall ($p < 0.001$) (Table.1). PASS subjects performed significantly better than FAIL subjects in QI, all four single-legged hop LSIs, and GRS ($p < 0.05$) 6-M after ACLR (Table 1). There were 15 subjects who completed the 6-M testing but did not complete the 12-M testing after ACLR. When their data were compared to those who completed the 12-M testing after ACLR, there were no significant differences for sex, graft type, PASS and FAIL ratio, age, and BMI ($p > 0.16$). However, there were significant differences for cross-over ($p = 0.01$), triple hop ($p = 0.049$), and 6-meter timed hop LSIs ($p = 0.03$) with subjects who did not completed the 12-M testing session demonstrated higher performance.

Table 1 Subject's demographics and RTAC variables for PASS and FAIL groups at 6-M after ACLR (Mean (SD)).

Variables	PASS (n=48)	FAIL (n=47)	P-value
Subjects # (women/men)	48 (11/37)	47 (21/26)	0.03
Age (year)	26.33 (9.39)	28.02 (11.81)	0.45
BMI (N/m ²)	24.71(3.17)	25.32(4.62)	0.49
Graft type (Autograft/Allograft)	19/29	17/30	0.60
QI (%)	103.02 (9.91)	91.07 (12.09)	<0.001
Single hop LSI (%)	97.74 (4.57)	88.10 (11.34)	< 0.001
Cross-over hop LSI (%)	97.92 (4.57)	93.71 (9.81)	0.01
Triple hop LSI (%)	97.3 (4.53)	92.78 (7.54)	0.001
6-meter timed hop LSI (%)	99.57 (5.22)	92.45 (8.73)	<0.001
KOS-ADLS (%)	96.86 (2.81)	97.70 (4.38)	0.37
GRS (%)	94.50 (4.85)	87.63 (12.00)	<0.001

2.7.1 Likelihood Ratios

At 12-M follow-up testing after ACLR 80 subjects completed the followed up testing, 31 subjects of those who PASS RTAC at 6-M after ACLR passed RTAC again 12-M after ACLR (Table 2). In addition, 15 subjects of those who FAIL on RTAC at 6-M after ACLR passed RTAC at 12-M after ACLR. Reasons for failing of these subjects on RTAC at 6-M after ACLR: six subjects scored <90% on QI; two scored <90% on QI and all hop LSIs; one scored <90% on all hop LSIs; one scored <90% single hop, triple hop, and 6-meter timed hop LSI; two scored <90% on single

hop and cross-over hop LSIs; one scored <90% on single hop LSI and QI; one scored <90% on single hop LSI, and one scored <90% on GRS.

In comparison, 23 subjects of those who FAIL on RTAC at 6-M after ACLR failed again on RTAC at 12-M after ACLR and 11 subjects of those who PASS RTAC at 6-M after ACLR failed on RTAC at 12-M after ACLR (Table 2). Reasons for failing of these subjects on RTAC at 12-M after ACLR: five subjects scored <90% on QI; two scored <90% on single hop, cross-hop, and triple hop LSIs; one scored <90% on single hop and cross-hop LSIs; one scored <90% on triple hop LSI and KOS-ADLS; one scored <90% on single hop LSI; and one scored <90% on GRS.

Table 2 Number of subjects who PASS and FAIL RTAC again 12-M after ACLR among groups.

	12-M PASS	12-M FAIL	Total
6-M PASS	31	11	42
6-M FAIL	15	23	38
Total	46	34	80

At 24-M follow-up testing after ACLR 60 subjects completed followed-up testing , 25 subjects of those who PASS RTAC at 6-M after ACLR passed RTAC again 24-M after ACLR. In addition, 14 subjects from those who FAIL on RTAC at 6-M after ACLR passed RTAC 24-M after ACLR (Table 3). Reasons for failing of these subjects on RTAC at 6-M after ACLR: five subjects scored <90% on QI; one scored <90% on QI and all hop LSIs; one scored <90% on all hop LSIs; one scored <90% on QI and 6-meter timed hop LSI; one scored <90% on QI and cross-over LSI; one scored <90% on single hop and cross-over hop LSIs; two scored <90% on single hop LSI; and two scored <90% on GRS.

In comparison, 13 subjects of those who FAIL on RTAC at 6-M after ACLR failed again on RTAC at 24-M after ACLR and 8 subjects of those who PASS RTAC at 6-M after ACLR failed on RTAC at 24-M after ACLR (Table 3). Reasons for failing of these subjects on RTAC at 24-M after ACLR: two subjects had injuries (one had ankle fracture and one had ACL re-tear); two subjects did not complete hop tests (one subject had medial knee pain and one subjects complained of knee instability and joint effusion); one subject scored <90% QI and cross-over hop LSI; three subjects scored <90 on QI.

The positive LHR's for those who PASS RTAC at 6-M after ACLR to PASS at 12-M and 24-M after ACLR were 2.08 and 1.68 respectively and the negative LHR's for those who FAIL on RTAC at 6-M after ACLR to FAIL at 12-M and 24-M after ACLR were 2.07 and 1.72 respectively ($P<0.05$) (Table 2 and 3). The positive LHR's for those subjects who FAIL RTAC at 6-M after ACLR to PASS RTAC at 12-M and 24-M after ACLR were 0.48 and 0.59 times respectively ($p<0.05$) and the negative LHR's for those who PASS RTAC at 6-M after ACLR to FAIL RTAC at 12-M and 24-M after ACLR were 0.48 and 0.57 times respectively ($p<0.05$).

Table 3 Number of subjects who PASS and FAIL on RTAC 24-M after ACLR

	24-M PASS	24-M FAIL	Total
6-M PASS	25	8	33
6-M FAIL	14	13	27
Total	39	21	60

2.7.2 Functional Performance Changes over Time

PASS group scored higher than FAIL group on all outcome measures at all follow-up testing sessions after ACLR except KOS-ADLS both groups had similar scores at all follow-up testing after ACLR. A significant group by time interaction was

found for single hop ($P=0.006$) and 6-meter timed hop LSIs ($p=0.037$) with FAIL group demonstrating a larger improvement specifically between 6-M to 12-M than PASS group. A significant main effect of group was detected for QI, cross-over hop, and triple hop LSIs ($p<0.01$). Main effect of time was detected for cross-over hop LSI, triple hop LSI, and GRS ($p<0.05$).

Performance-based measures:

Quadriceps Index:

There was a significant main effect of group for the QI ($P<0.01$). QI measure was significantly different between PASS and FAIL groups 6-M ($p<0.001$), 12-M ($p<0.001$), and 24-M ($p=0.04$) after ACLR. Neither FAIL nor PASS groups improved significantly between 6-m and 12-M and 6-M and 24-M follow-up testing after ACLR ($p>0.05$) (Figure 4).

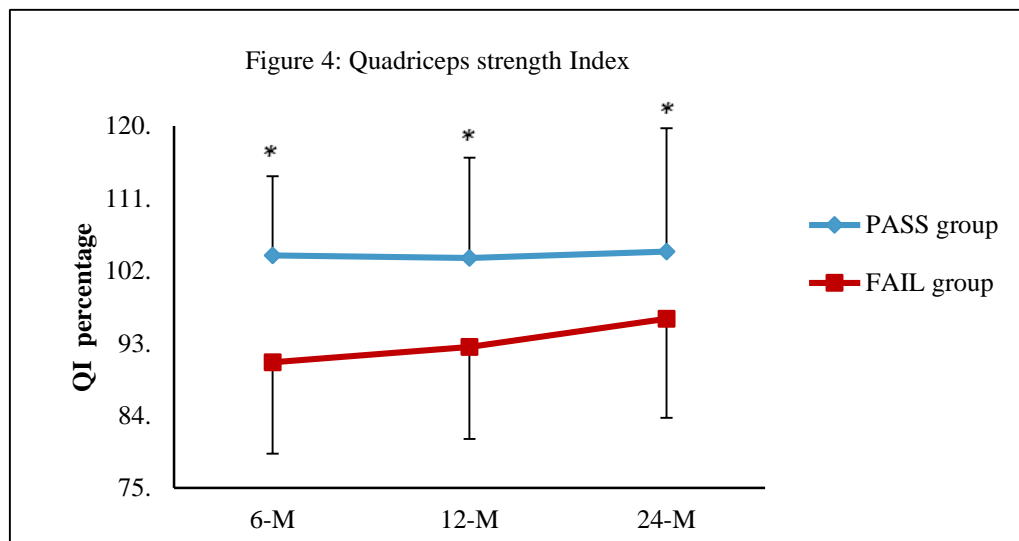


Figure 4 QI of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P< 0.05$))

Hop performance LSIs:

A significant group by time interaction was found for single hop LSI ($P=0.006$). Post hoc test shown that single hop LSI was significantly different between PASS and FAIL groups at 6-M ($p<0.001$) and 24-M ($p=0.02$) after ACLR (Figure 5). PASS and FAIL groups improved their performance on single hop LSI over time with the largest improvement in the FAIL group between 6-M and 12-M after ACLR. Post hoc test shown that only FAIL subjects improved significantly on single hop LSI between 6-M and 12-M ($p=0.02$) and between 6-M and 24-M ($p<0.01$) after ACLR (Figure 5).

Significant main effect of group and main effect of time were found for cross-over hop LSI ($p<0.05$). Cross-over LSI was significantly different between PASS and FAIL groups only at 6-M after ACLR ($p=0.01$). PASS and FAIL groups significantly improved in cross-over hop LSI over time after ACLR ($p<0.05$) (Figure 6). Significant main effect of group and main effect of time were found for triple hop LSI ($p<0.05$). Triple hop LSI was significantly different between groups at 6-M ($p=0.001$) and 12-M ($p=0.02$) after ACLR. PASS and FAIL groups significantly improved in triple hop LSI over time after ACLR ($p<0.05$) (Figure 7).

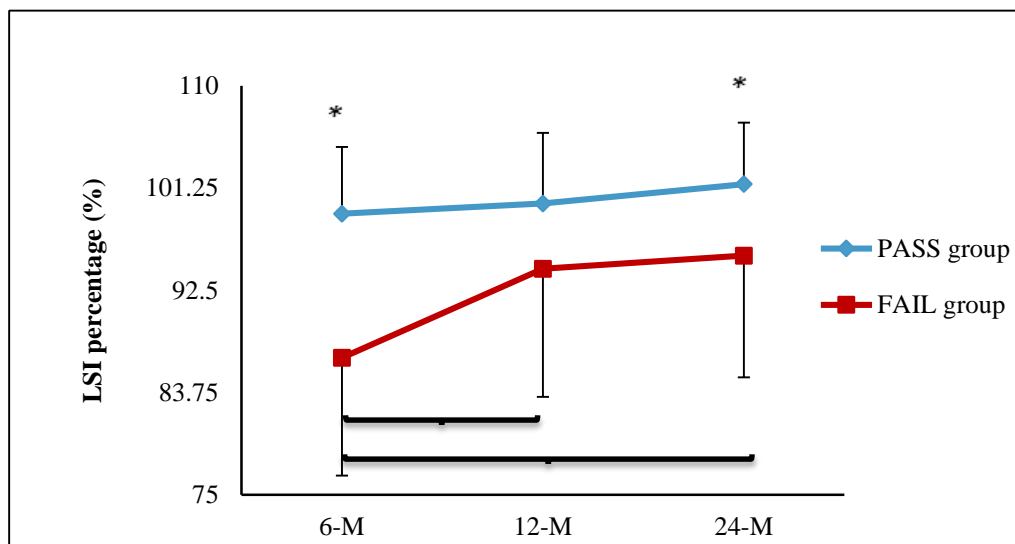


Figure 5 Single hop LSI of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P< 0.05$))

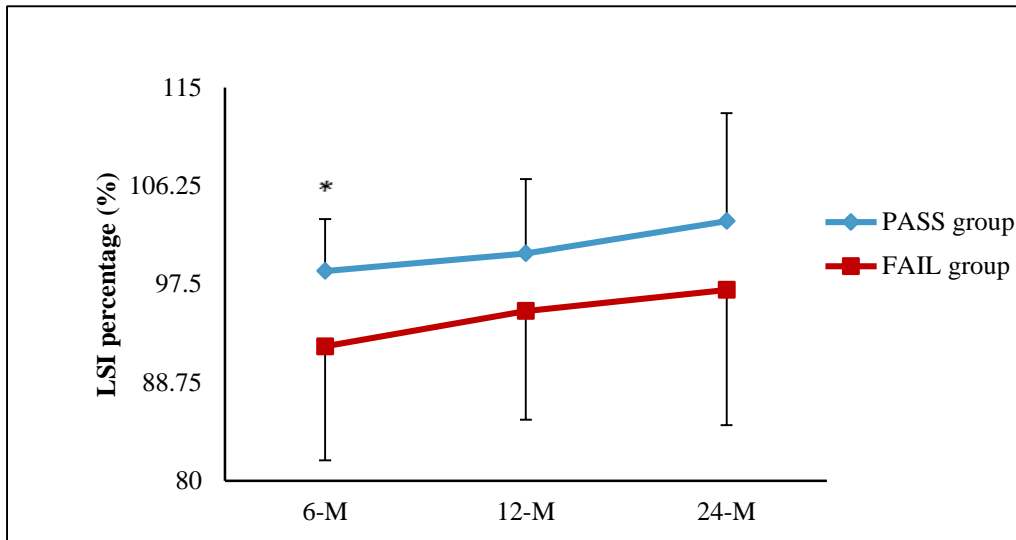


Figure 6 Cross-over hop LSI of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P < 0.05$))

A significant group by time interaction was found for 6-meter timed hop LSIs ($p=0.037$). Post hoc test shown that 6-meter timed hop LSI was significantly different between groups only at 6-M ($p < 0.001$) after ACLR with PASS group hopped faster than FAIL group at 6-M follow-up testing after ACLR. Post hoc test shown that FAIL group improved significantly on 6-meter timed hop LSI between 6-M and 12-M time interval after ACLR ($p < 0.01$) (Figure 8).

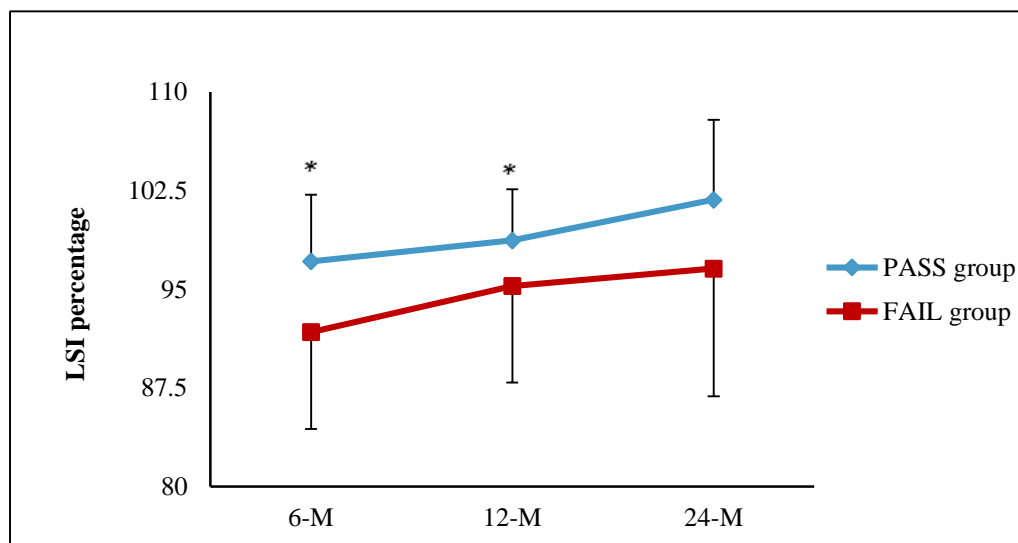


Figure 7 Triple hop LSI of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P < 0.05$))

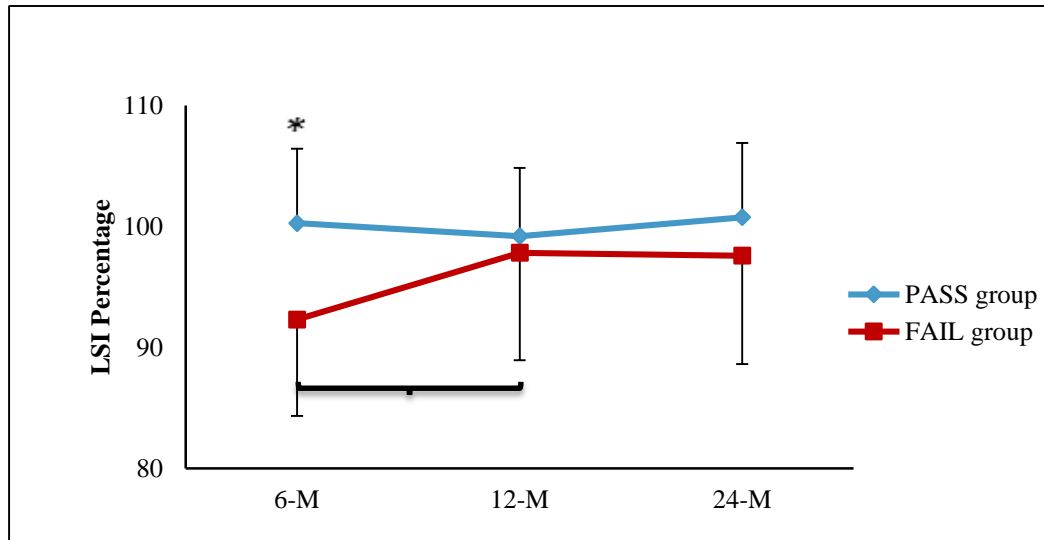


Figure 8 6-meter timed hop LSI of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P < 0.05$))

2.7.3 Patient-Reported Measures

PASS and FAIL groups had similar scores on KOS-ADLS at all follow-up testing time points ($p > 0.05$). Neither PASS nor FAIL improved their KOS-ADLS scores significantly between the follow up time points after ACLR ($p > 0.05$) (Figure 9). Main effect of time was detected for GRS ($p < 0.05$). GRS was significantly different between PASS and FAIL groups only at 6-M after ACLR ($p < 0.001$). PASS and FAIL groups improved their scores significantly over time (Figure 10). FAIL group improved their GRS scores significantly between 6-M and 12-M ($p = 0.04$) and

between 6-M and 24-M ($p=0.01$) after ACLR, while PASS group improved significantly between 6-M and 24-M after ACLR ($p=0.03$) (Figure 10). The greatest GRS improvement by FAIL group was achieved between 6-M and 12-M after ACLR.

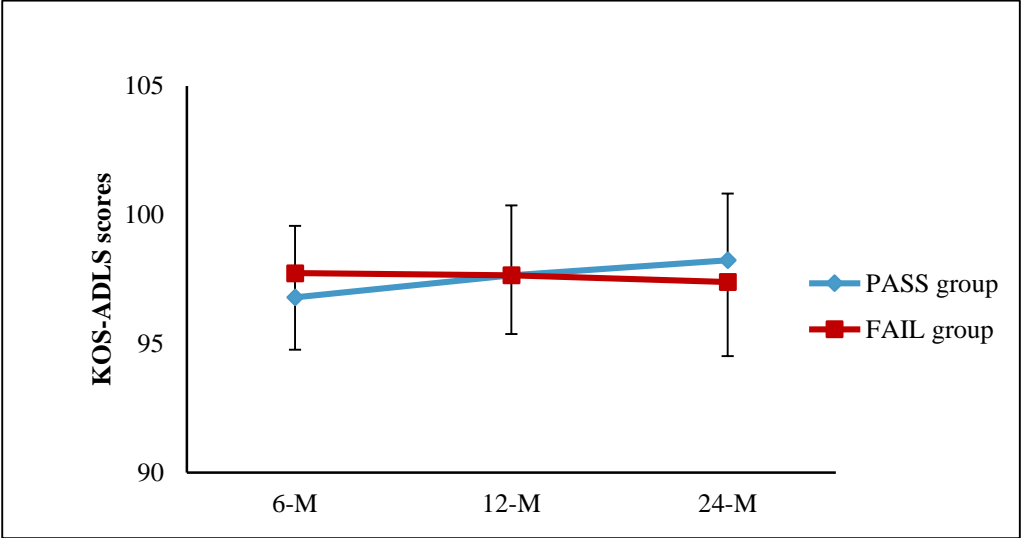


Figure 9 KOS-ADLS of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P < 0.05$))

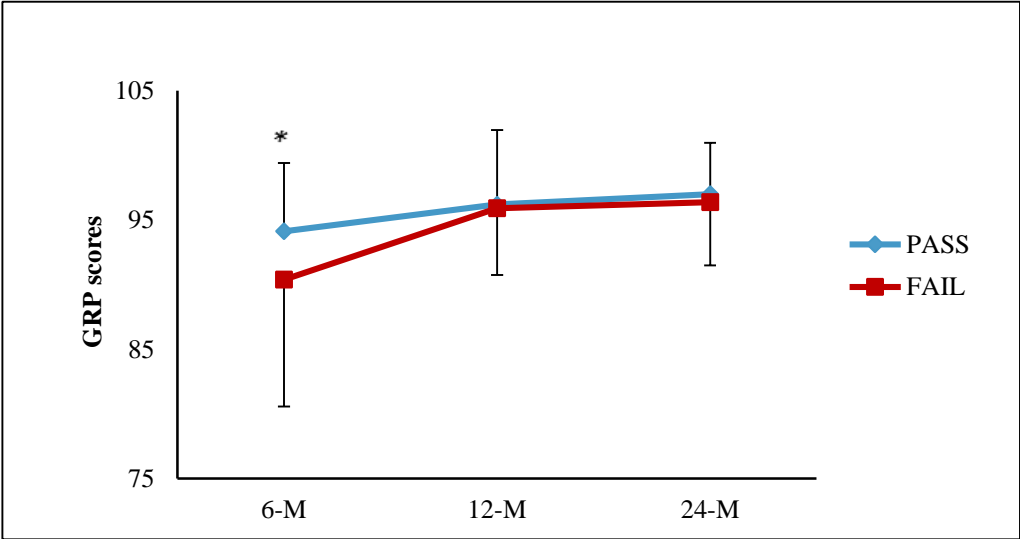


Figure 10 GRS of PASS and FAIL groups at 6-M, 12-M and 24-M after ACLR (Mean (SD); (*: Significant difference between groups $P < 0.05$))

2.8 Discussion

The purpose of this study was to investigate performance-based and patient-reported measures 12-M and 24-M after ACLR between subjects who passed or failed on RTAC at 6-M after ACLR, and to further investigate how their functional performance and patient-reported measures change over time. The results of this study show that PASS group achieved higher knee performance-based and patient-reported scores on RTAC early after ACLR compared to FAIL group and continued to maintain higher knee function up to 24-M after ACLR. FAIL group improved their scores on knee performance-based and patient-reported measures between 6-M and 12-M follow-up testing after ACLR, and continued to improve 24-M after ACLR.

Our strict RTAC of passing all seven performance-based and patient-reported measures were used to evaluate subjects' self-reported knee function and limb-to-limb movement symmetry. At 6-M follow-up testing after ACLR, only half of subjects demonstrated normal quadriceps-strength and hop-performance limb symmetry indexes and scored $\geq 90\%$ on patient-reported measures. The total percentage of subjects who PASS RTAC at 6-M after ACLR increased at both 12-M and 24-M follow-up testing after ACLR. Subjects who PASS RTAC 6-M after ACLR were two times more likely to PASS RTAC again at 12-M and 24-M after ACLR than those who FAIL. In comparison, the total percentage of subjects who FAIL on RTAC at 6-M after ACLR continued to be within the same range. Subjects who FAIL on RTAC 6-M after ACLR were 2.7 and 1.72 times more likely to FAIL on RTAC again at 12-M and 24-M respectively after ACLR than those who PASS. The results of this study reveal that subjects demonstrating normal quadriceps strength and hop limb-to-limb symmetry, and self-reported knee function 6-M after ACLR are more likely to exhibit normal functional performance-based and patient-reported knee function 12-M and

24-M after ACLR. By comparison, subjects demonstrating quadriceps strength and hop limb-to-limb asymmetry, and poor self-reported knee function at 6-M after ACLR are more likely to demonstrate similar performance-based and self-reported knee function 12-M and 24-M after ACLR. Previous studies by Di Stasi and colleagues⁹⁶ and Hartigan and colleagues²⁴ reported similar results to our study, nearly half of the subjects passing RTAC 6-M after ACLR. A study by Logerstedt and colleagues²⁵ indicated that subjects improved between baseline and 6-M follow-up testing after ACLR and continued to improve from 6-M to 12-M after ACLR, however, the authors did report the percentage of subjects who achieved $\geq 90\%$ on individual outcome measures but not as collective criteria. Subjects who still demonstrate limb-to-limb asymmetry after ACLR are of main concern to clinicians as there may be a lower likelihood of this group to return to preinjury activity levels as well as they may have a higher risk for secondary ACL injuries⁹⁵. The results of this study highlight the importance of using RTAC to identify subjects who are more susceptible to demonstrate persistent poor knee function and limb-to-limb asymmetry after ACLR and to compel clinicians to consider individualized extended treatment programs.

The results of this study showed that FAIL group improved their functional performance on several outcome measures. This improvement, however, did not result in all subjects passing RTAC variables collectively as 28.7% and 21.6% of subjects continued to fail again on the criteria collectively at 12-M and 24-M respectively after ACLR. In contrast, a select number of subjects who failed on RTAC at 6-M after ACLR were successful to pass RTAC at 12-M and 24-M after ACLR. Subjects who FAIL RTAC at 6-M after ACLR were 0.48 and 0.59 times more likely to PASS RTAC at 12-M and 24-M after ACLR respectively. These results suggests that those

subjects who failed on the criteria 6-M after ACLR are more than 50% more likely to pass RTAC again by restoring normal knee functional performance and limb-to-limb movement symmetry at 12-M and 24-M after ACLR. Many of those subjects that failed 6-M after ACLR scored less than 90% on one or two of RTAC variables. In fact, the majority of subjects passed RTAC at 12-M and 24-M after ACLR mainly due to improvement in quadriceps strength. Therefore, these subjects had high potential to pass RTAC especially if they continued participation in an extended training program..

Disappointingly, the study also showed that some subjects who passed RTAC at 6-M after ACLR failed on RTAC at 12-M or 24-M after ACLR. Subjects who PASS RTAC at 6-M after ACLR were 0.48 and 0.57 times to FAIL RTAC at 12-M and 24-M after ACLR respectively. The reasons for failing on RTAC were due to quadriceps strength deficits, poor performance on hop tests, or scoring low on patient-reported measures (mainly GRS). These subjects did not maintain normal quadriceps strength and knee functional performance as they may have quitted participation in functional or sport activities. This may be due to fact that most of subjects were students who may have graduated or moved out for work opportunity, family and work commitments, less opportunity to participate in sport activities, or fear from sustaining further knee injuries ^{85,104}.

In this study, the data were reported for both PASS and FAIL groups using the group's means but not the individual score of each subject on each of RTAC variables. Therefore, while the reported group's means exceed 90% on one or more of the RTAC variables, that does not necessarily indicate that the subjects in the FAIL group passed RTAC. In this study, subjects were classified as FAIL if they scored less than 90% on any one of the RTAC variables. Quadriceps strength and single-legged hop

performances limb-to-limb asymmetries are prevalent after ACL injury and can persist after ACLR ^{66,105-107}. Underlying quadriceps strength deficits in the reconstructed limb may contribute to poor hop performance as subjects with quadriceps weakness hop for shorter distances and slower on timed hop test ²⁵. In this study, the main reasons for those subjects who PASS RTAC at 6-M after ACLR but failed on the criteria at 12-M and 24-M after ACLR was quadriceps strength deficit as these subjects demonstrated quadriceps strength deficit larger the 10% compared to the uninvolved limb.

Additionally, patient failed on RTAC at 12-M and 24-M after ACLR due to poor functional performance on hop tests, or due to recent lower extremity injuries. These subjects may have failed on RTAC at 12-M and 24-M after ACLR as they may choose to stop participation in functional or sport activities. Additionally, the population of this study included mainly colligates students who may have graduated or moved out to other school or for work. Some of subjects may stop participation in functional or sport activities due to changes in life style, opportunity to participate in activities, or fear of sustaining further injuries¹⁰⁴.

The presence of limb-to-limb asymmetry after ACLR can impact lower extremity performance, subsequently magnified in vigorous activities such as competitive interactions with opponents and being in less controlled environments ^{20,43}. Consequently, limb-to-limb asymmetry may predispose subjects' to re-injury and lead to the initiation and progression of osteoarthritis pathomechanics for the knee joint ^{49,108}. Kinematic and kinetic asymmetries are linked to the development of knee osteoarthritis ^{50,108,109} and predisposed factors for a second ACL injury ⁴³. Subjects with limb-to-limb asymmetry tend to overuse the uninjured limb, resulting in overuse

injuries to that limb^{67,110}. By contrast, subjects with limb-to-limb asymmetry may underuse the injured limb due to the lack of confidence.

Significant group-by-time interaction was only found for single hop and 6-meter timed hop LSIs, however, subjects in PASS and FAIL groups improved in quadriceps strength, cross-over hop and triple hop LSIs, and GRS over time. The improvements between 6-M, 12-M and 24-M most likely resulted from subjects' participation in both functional and athletic activities that include repetitive running, jumping, landing, and turning movements. By contrast, results of the KOS-ADLS shows that subjects in both groups did not change over time, this is not surprising in light of KOS-ADLS questionnaire that asks about basic daily living activities performed by most subjects without difficulty at the time of follow-up testing.

A pattern of improvement on some of outcome measures was seen for FAIL subjects after ACLR; the majority of those subjects achieving the greatest improvement between 6-M and 12-M interval after ACLR. This improvement can be explained by the fact that FAIL subjects initially scored lower on performance-based tests and patient-reported knee function measures at 6-M after ACLR. Therefore, they had more potential for improvement compared to the PASS subjects who did not show nearly the degree of improvement as a result of less room of improvement on outcome measures of interest. A study using the same RTAC after ACLR reported that 50% of athletes demonstrated normal knee functional and limb movement symmetry on RTAC at 6 months and more than 75% at 1 year after ACLR²⁴.

The ultimate goal of the ACLR is restoration of mechanical knee stability, normal knee function, and symmetrical limb movement to facilitate returning to preinjury activities^{28,62,91,111}. The results of this study allow identifying those variables

that patients continue to fail at in after ACLR which can be addressed through providing appropriate intervention. In light of our study results, those subjects planning to return to their preinjury activities but who fail to restore limb-to-limb symmetry might need to participate in an extended rehabilitation program. Clinicians might consider administration of an extended training program that includes intensive quadriceps strengthening, agility drills, and plyometric training to ensure restoration of limb-to-limb symmetry before patient reintegrate into vigorous activity. If, however, subjects still exhibit limb-to-limb asymmetry after participating in an extended rehabilitation program, they might need to be advised to change from or modify their activities to less high-risk activity. The reasons for those subjects who FAIL on RTAC at 6-M after ACLR but PASS on RTAC at 12-M and 24-M after ACLR include improving quadriceps strength, knee functional performance on hop tests, and rating their knee functional higher on patient-reported measures. Most of these subjects failed on one or two of RTAC variables. Therefore, they possess knee functional performance similar to PASS group but they did not pass on all RTAC collectively. These subjects may improve their strength and functional performance through participation in functional and sport activities.

Though we used the time basis approach in the study design for the follow-up testing which is a limitation for the study, the group factor used in the analysis was based on classifying the subjects on a criterion basis (i.e. PASS and FAIL). In addition, we solely use criterion basis to clear subjects to return gradually into their perjury activity levels. Therefore, the results of this study suggest testing subjects on an individual basis using performance-based and patient-reported measures rather than using time-based criteria as a guideline to determine patients' readiness to return to

preinjury activities. In addition, testing subjects on a regular basis using a battery of tests following rehabilitation is seen to be a preferred method to assess knee functional performance and limb-to-limb movement symmetry and to identifying subject with high risk for further knee injuries.

2.9 Limitation

The population of this study was limited to individuals who participated in level I or II activities and underwent ACLR and therefore these findings cannot be generalized for individuals participating in less demanding activity or to those having ACL rupture who chose to be managed non-operatively. In this study we used 6-M time points after ACLR after ACL as baseline testing instead of using time of passing the RTAC, the reason being that passing RTAC varied among patients. In addition, there were subjects who dropped out of the study and did not return for the follow-up testing. Some of the subjects who dropped out of the study due to scholastic transition as majority of the study's population are colligate students who have moved away after finishing college or for work. Additionally, reasons related to changes in life style, lower opportunity to participate in activities, fear of sustaining another knee injury, or socioeconomic status^{85,112}. In this study, few subjects sustained either graft tear or other lower extremities injuries.

2.10 Conclusion

The findings of this study revealed that subjects who FAIL on RTAC 6-M after ACLR were more likely to demonstrate impaired knee function and limb-to-limb movement asymmetry 12-M and 24-M after ACLR. However, a majority of FAIL subjects did improve knee performance, limb-to-limb symmetry, and patient-reported

measures during the first year after ACLR. Using a battery of RTAC that include performance-based and patient-reported measures can help identify subjects having limb-to-limb asymmetry and therefore should be utilized to identify these persistent dysfunctions.

Chapter 3

KNEE FUNCTIONAL PERFORMANCE SIX MONTHS PREDICTS RETURN TO PARTICIPATE IN THE SAME PREINJURY ACTIVITY LEVEL 12 AND 24 MONTHS AFTER ACL RECONSTRUCTION

3.1 Abstract

Background: Assessing athletes' readiness is a key component for successful return to preinjury activity level after anterior cruciate ligament reconstruction (ACLR). A battery of return to activity criteria (RTAC) that emphasize normal knee function and limb movement symmetry has been used to clear athletes to return to preinjury activity level. The purpose of this study was (1) to investigate whether RTAC variables at 6 month (6-M) after ACLR can predict return to participate in the same preinjury activity level 12 months (12-M) and 24 months (24-M) after ACLR, and (2) to investigate which individual or a combination of RTAC variables 6-M after ACLR predicts return to participate in the same preinjury activity level 12-M and 24-M after ACLR.

Methods: One-hundred and eight level I or II participants with ACLR participated in the study. At 6-M after ACLR, all participants completed performance-based tests (isometric quadriceps strength (QI) and four single-legged hop tests: single hop, cross-over hop, triple hop, and 6-meter timed hop) and two patient-reported measures (Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS) and the Global Rating Score of perceived knee function (GRS)). Limb symmetry indexes (LSI) were calculated as the ratio of the performance of the involved limb to uninjured limb x 100 for the performance-based measures. Participants who scored \geq 90% on all RTAC variables were classified as PASS group and those who scored $<$ 90% on any of RTAC variables were classified as FAIL. At 12-M and 24-M after

ACLR, participants were asked if they had returned to participate in the same preinjury activity level or not at 12-M and 24-M after ACLR.

Results: Thirty (81.1 %) and 27 (84.4%) participants of PASS group returned to participate in the same preinjury activity level at 12-M and 24-M respectively after ACLR. Six-months single hop, triple hop, and 6-meter timed hop LSIs, KOS-ADLS, and GRS were significant predictors of return to participate in the same preinjury activity level at 12-M after ACLR ($p < 0.05$). The combined of 6-meter timed hop LSI, GRS, single hop LSI, triple hop LSI, and KOS-ADLS explained 27% of the variance ($p = 0.008$). The positive likelihood ratio of PASS group to return to the same preinjury activity level at 12-M after ACLR was 2.71, while the negative likelihood ratio of FAIL group to not return to the same preinjury activity level at 12-M after ACLR was 1.99 ($p < 0.001$). All single-legged hop LSIs were individually significant predictors of return to participate in the same preinjury activity level at 24-M after ACLR ($P < 0.05$). The combination of single-legged hop LSIs at 6-M after ACLR explained 38% of the variance ($p < 0.002$). The positive likelihood ratio of PASS group to return to the same preinjury activity level at 24-M after ACLR was 2.70, while the negative likelihood ratio of FAIL group to not return to the same preinjury activity level at 24-M after ACLR was 2.31 ($p < 0.009$).

Discussion: RTAC variables can predict return to participate in the same preinjury activity levels at both 12-M and 24-M after ACLR. RTAC variables explain more than one-fourth to one-third of the return to participate in the same preinjury activity level variance at both 12-M and 24-M respectively after ACLR. Participants who returned to participate in the same preinjury activity level 12-M and 24-M after ACLR are more likely to demonstrate normal limb-to-limb symmetry and report high

global knee function at 6-M after ACLR. While those who didn't return are more likely to exhibit limb asymmetry and poor knee function which might create barriers for returning to preinjury activity levels.

3.2 Introduction

Anterior cruciate ligament (ACL) is the most common injured ligament in the knee joint during sport activities that include pivoting, jumping, and cutting movements^{69,88}. ACL rupture is a devastating injury to the knee joint that prevents athletes from participating in both daily living and high physical activities. Additionally, athletes with ACL rupture required an extended time before returning to the preinjury activity level. Commonly seen impairments following ACL rupture includes frequent episodes of dynamic knee instability, quadriceps strength deficits, neuromuscular dysfunction, limb-to-limb movement asymmetry, and biomechanical mal-adaptations^{7,50,109}. Early ACL reconstruction (ACLR) is the current gold standard treatment for young, active athletes who desiring to return to high-level activities after ACL rupture⁶². The current clinical practice guidelines recommends an early and progressive post-surgical ACL-rehabilitation program to resolve knee impairments and to restore normal knee function and symmetrical limb-to-limb movement that facilitate successful return to multidirectional activities²². The recent studies, however, report that the rate of return to preinjury activity level among athletic individuals is poor and greatly varied after ACLR¹¹³⁻¹¹⁵. The attempts to identify factors that evaluate athletes' physical capacity and ultimately contribute to the return to preinjury activity level are under investigated.

In a recent systemic review and meta-analysis study reports 81% of athletes returned to any type of sport activities and 55% of athletes returned to competitive

level sport at different time points after ACLR surgery⁶⁸. While, only one-third of athletes returned to full competition in sports activity at one year after ACLR⁹⁰. Multiple factors reported in literature that might be associated with the low rate of returning to preinjury sport activities, some of these factors are non-modifiable by rehabilitation and are related to the athletes' demographic and injury (i.e. gender^{70,116}, age¹¹⁶, preinjury activity level¹¹⁷, concomitant knee injuries, and time from surgery^{117,118}). Other factors are modifiable and related to physical function (i.e. quadriceps strength deficit, effusion, knee range of motion deficit, psychological factors¹⁰⁴, neuromuscular dysfunction, and aberrant biomechanical patterns⁴³). These modifiable factors can be addressed by providing an appropriate intervention in purpose to promote the functional recovery and maximize the athletes' functional capacities that are required to meet the physical demands of their sport activities.

Other factor might also be associated with the low rate of returning to the preinjury activity level include the criteria that are used to clear to return to the preinjury activity level. Currently, there is no universal comprehensive set of objective criteria that are used to determine athletes' functional readiness among researchers and clinicians. One approach that has been used for determining athlete's readiness to participate in preinjury activity level is solely based on the time from surgery; orthopedic physicians advocate that 6-9 months after ACLR is the typical time to return to preinjury activity level^{61,73}. Barber-Westin et al reported that 60% of studies report using time from surgery and 15% of studies report using the time from surgery along with subjective factors to determine readiness to return to unrestricted sports activities after ACLR. Further, only 13% of studies report using objective criteria (i.e.

lower extremity muscle strength, limb movement symmetry, knee range of motion, and joint effusion)⁷⁶.

The University of Delaware Physical Therapy clinic use a strict return to activity criteria that emphasizes limb-to-limb symmetry and good knee function to quantitatively determine clearance to return to activities. The return to activity criteria include performance-based and patient-reported measures that were instituted as a criterion-basis approach to guide releasing athletes to return to multidirectional activities^{22,24}. These criteria are sensitive to knee functional changes over time and can provide clinicians with clinically relevant information about patients' responses to different therapeutic interventions.

Performance-based measures that capture knee performance and functional deficits can predict patient-reported knee function measures after ACLR³⁴. Logerstedt and colleagues reported that single-legged hop tests conducted 6 months after ACLR predicted the likelihood of normal and poor patient-reported knee function 12 months after ACLR³⁴. Only explanatory variables, however, that include patient demographics, concomitant injuries, and treatment variables that are associated with return to preinjury activity level after ACLR have been investigated. Though, these explanatory variables can predict patient-reported measures, they do not fully explain the variance in the knee functional after ACLR. Dunn and colleagues⁸⁵ revealed that higher activity level 2 year after ACLR was associated with participating in high level activity and lower body mass index at the time of injury, while women, smoking within 6 months of prior to the surgery, and revision ACLR were associated with lower activity level⁸⁵. Additionally, Ardern and colleagues reported returning to preinjury activity level is favored in athletes with symmetrical hopping performance

and in athletes who participate in running, pivoting decelerating, and pivoting activities⁶⁸.

The ability of RTAC variables to predict return to participate in the same pre-injury activity level after ACLR has not been investigated. Additionally, it is unknown whether an individual or a combination of return to activity criteria variables after ACLR contributes to the ability to predict return to the same preinjury activity levels in the future. Therefore, the purpose of this study was (1) to investigate whether return to activity criteria variables predict return to the same preinjury activity level 12 months (12-M) and 24 months (24-M) after ACLR, and (2) to investigate which individual or a combination of return to activity criteria variables 6 months (6-M) after ACLR predicts returning to the same preinjury activity levels 12-M and 24-M after ACLR.

3.3 Methods

One-hundred and eight participants with an ACLR were pulled out from an ongoing, prospective, longitudinal cohort study. All participants were between the ages of 15 and 55 years. All participants were regular participants in level I or II sport activities that involves jumping, cutting, pivoting, and lateral movements (i.e. soccer, football, rugby, tennis, ice hockey, and wrestling) for at least 50 hours/year prior to their injury⁷. Participants with concomitant ligamentous injury, repairable meniscal injury, full-thickness articular cartilage damage, or a history of serious ipsilateral or contralateral lower extremity injury (i.e. fracture) were not enrolled into this study. Sixty-eight (63.2%) of participants received 10-sessions while the rest received at least 4-sessions of pre-operative rehabilitation training that included progressive quadriceps strengthening and specific perturbation training as described by Fitzgerald et al^{5,97}.

Ligament reconstructions were performed on 108 participants (71%) using a soft tissue allograft (n=69), a semitendinosus-gracilis autograft (n=37), or a bone patellar tendon bone autograft (n=2). Post-operatively, all participants underwent a supervised, progressive post-operative rehabilitation protocol that included early resolution of joint effusion, range of motion deficits, quadriceps strength impairments, and activity limitations. Neuromuscular and weight-bearing training activities were integrated early in the post-operative rehabilitation process⁶⁵. Participants were progressed through pre-operative and post-operative rehabilitation as they met clinical milestones described by Adams et al²². Data were collected on participants at 6-M, 12-M, and 24-M after ACLR. The study was approved by the University of Delaware Institutional Human Subjects Review Board. All participants provided written informed consent for participation in this study. One-hundred and eight participants were included in the study, however, performance-based and patient-reported data were available for 95 participants (Men: 63; Women: 32; mean age: 27.14 \pm 10.59) at 6-M (mean: 6.26 \pm 0.81 months). Eighty participants (Men: 51; Women: 29) at 12-M (mean: 12.44 \pm 1.13 months) and 60 participants (Men: 38; Women: 22) at 24-M (mean: 25.1 \pm 4.16 months) returned for follow-up testing and reported whether they have returned to participate in the same preinjury activity level or not. Data were unavailable for 13 participants at 6-M, 15 participants at 12-M, and for 20 participants at 24-M after ACLR with reasons for missing data illustrated in Figure 11.

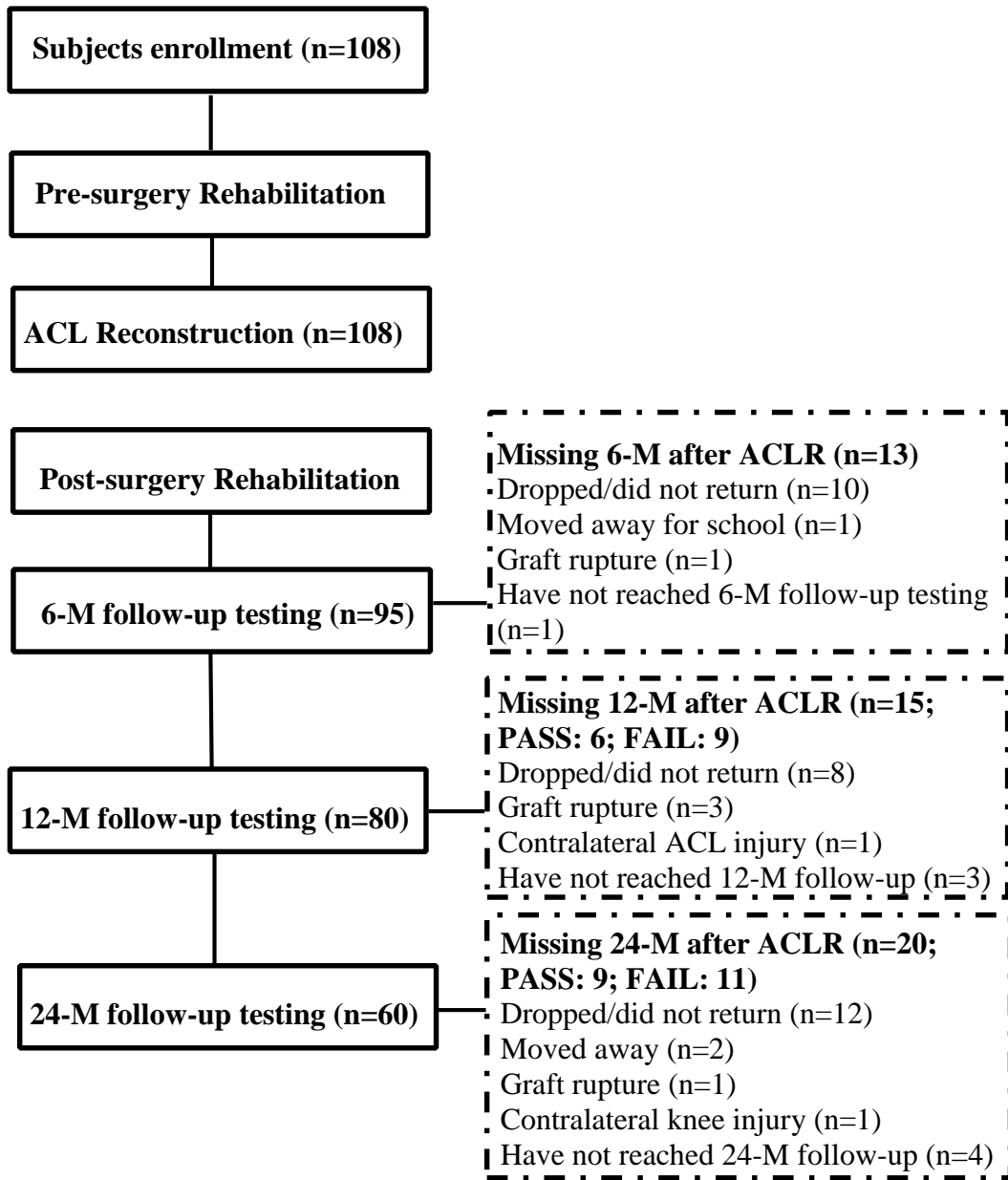


Figure 11 Flow diagram for subject participation at 6-M, 12-M and 24-M follow-up testing after ACLR.

3.4 Testing

Participants completed a battery of RTAC that involve both performance-based tests and patient-reported measures of knee function including isometric quadriceps strength testing, four single-legged hop tests, Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS), and Global Rating Score of perceived knee function (GRS) at 6-M after ACLR ^{25,30}. At 12-M and 24-M follow-up after ACLR, participants answered a question that asks whether they have returned to participate in the same preinjury activity level or not.

3.4.1 Performance-Based Measures

Isometric quadriceps strength was measured using a maximal voluntary isometric contraction (MVIC) of the quadriceps muscles ⁹⁸ on an electromechanical dynamometer (Kin-Com, Chattanooga Corp, Chattanooga, TN). Participants were seated with their hip and knee flexed to 90° with stabilization at the hip, knee and ankle (Figure 12). Participants were asked to perform three-practice trials (two at submaximal and one at maximal effort). All participants were instructed about the testing procedure. Approximately three seconds into the contraction, participant verbally encouraged to maximally contracting their quadriceps muscle. Testing was performed on the uninvolved limb followed by the involved limb. Quadriceps index (QI) was calculated by dividing the involved quadriceps force by the uninvolved quadriceps force multiplied by 100. At 6-M testing after ACLR, one subject did not complete quadriceps strength testing due to complaints of patellofemoral pain.



Figure 12 Maximal voluntary isometric contraction

Single-legged hop performance testing was measured using a series of single-legged hop tests⁹⁹: single hop, triple cross-over hop, and triple hop for distance and 6-meter timed hop (Figure 13). Participants were required to demonstrate symmetrical knee range of motion, minimal knee joint effusion¹⁰⁰, $QI \geq 80\%$, and no complaints of pain with stationary hopping on the involved limb prior to hop testing. All single-legged hop tests at 6-M after ACLR were performed with participants wearing a functional knee brace. All participants performed two practice trials followed by two measurement trials of each hop test on both limbs. Measurement trials were counted if participants maintained their balance during landing without touching the ground with the other foot. Hop performance limb symmetry indexes (LSIs) for distance were calculated as the percentage of the mean involved limb hop distances divided by the mean uninvolved limb hop distances for each individual hop test for distance

multiplied by 100. The 6-meter timed hop LSI was calculated as the percentage of the mean uninvolved limb hop time divided by the mean involved limb hop time. At 6-M follow-up testing five participants did not complete single-legged hop tests (one subject had increased knee joint effusion (2+ effusion), two participants had $QI < 80\%$, one subject reported patellofemoral pain, and one subject reported foot pain and knee joint effusion (1+ effusion)).

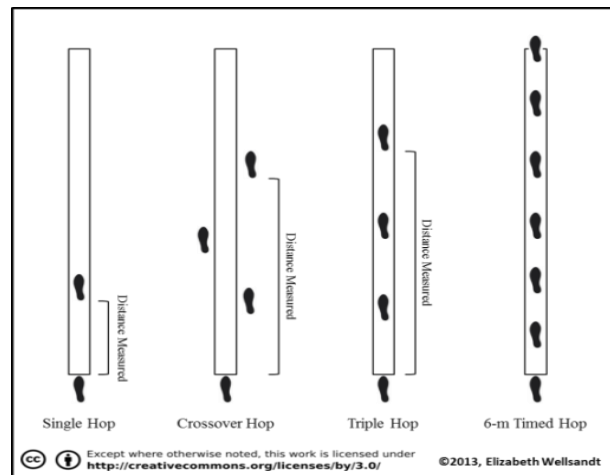


Figure 13 Four single-legged hop tests

3.4.2 Patient-Reported Measures

Participants filled out patient-reported questionnaires (KOS-ADLS and GRS) after all performance-based testing were completed, so participants have better perception of their knee functional performance. The KOS-ADLS is a patient-reported measure consisting of 14-items regarding the participants' perception of their knee symptoms and functional limitations related to ACLR and how these limitations affect their ability to perform activities of daily living such as walking, ascending and descending stairs, kneeling, sitting, and squatting⁴⁰. The KOS-ADLS has been shown

to be a reliable, valid, and responsive measure for assessing functional limitations of the knee, with high intraclass coefficients of 0.97 and test-retest reliability ¹⁰². Scores for The KOS-ADLS are reported as a percentage of the subject's points divided by the total possible points multiplied by 100. The GRS is used to assess participants' current knee functional performance. The GRS is a one-item question that asks participants to rate their current knee function on a scale from 0% to 100%, with 0% being the inability to perform any activity and 100% being their level of knee function prior to injury, including sports activities. It has been reported that analogue GRS has a high test-retest intraclass coefficients of 0.96 ¹⁰³. At 12-M and 24-M follow-up after ACLR, participants answered the following question "Have you returned to the same level of sports or recreational activities as before your injury?". This question is a single yes or no question asking if they had returned to participate in the same preinjury activity level or not.

3.5 Return to Activity Criteria

All participants were eligible to start testing for returning to their preinjury activity level on our battery of tests as early as 12 weeks after ACLR and once their impairments had resolved. All participants were cleared to begin gradual reintegration into their preinjury activity once they achieved at least 90% on all RTAC variables: QI, all four single-legged tests, KOS-ADLS, and GRS. Participants who achieved scores of 90% or more on all RTAC at 6-M were categorized as PASS and those who failed to achieve 90% on any of the RTAC variables were categorized as FAIL. In addition, participants who did not complete the hop tests due to quadriceps weakness (QI<80%), pain, or did not trust their knee/fear of reinjury were also classified as FAIL. Those participants who failed on RTAC were given 3-4 weeks to improve their

muscular strength and functional performance before retesting. A cut off ratio of 90% of the performance of the involved limb to uninjured limb on RTAC was chosen to determine within normal knee function, quadriceps strength, and limb symmetry during functional tasks^{24,86,119}. These RTAC were only used to classify participants as PASS or FAIL 6-M after ACLR.

3.6 Statistical Analysis

Independent t-test was used to determine differences between PASS and FAIL groups for participant's demographics and RTAC variables at 6-M after ACLR. Chi square test was used to determine whether women to men participants were significantly different between groups. Likelihood ratios were used to determine the relationship between participants who did return to participate in the same preinjury activity level at 12-M and 24-M after ACLR and those who did not return among PASS and FAIL groups. An initial binary logistic regression model was used to evaluate whether RTAC variables at 6-M can predict return to participate in the same preinjury activity level 12-M and 24-M after ACLR as well as to evaluate the proportion that each of RTAC variable can predict the outcome of interest. Data from both groups was used in the logistic regression. The QI variable was not used in the prediction model of this study due to the fact that QI variable was used as an assessment measure to determine the participants' eligibility to perform the single-legged hop tests (participant were not allowed to perform the single-legged hop tests unless they demonstrated 80% or more on QI). Based on that, we anticipated the QI to have less variability which in turn will reduce the ability of QI to predict the outcome of interest. Only those significant univariate predictor variables of RTAC were entered into a second regression model, with the variables entered into this model in the order

of most variance explained to least variance explained (R^2 : Nagelkerke R square). All data were analyzed with SPSS 20.0 (IBM Company, Chicago, Illinois) with a significance level of 0.05 set a priori.

3.7 Results

Complete data were available for 95 participants (48 PASS, 47 FAIL; mean PASS time: 5.69 +2.78 months) at 6-M, 80 participants at 12-M, and 60 participants at 24-M after ACLR. There was no difference in age and BMI between PASS and FAIL groups ($p>0.05$), however, the number of women participants was significantly higher in FAIL group at 6-M after ACLR ($p=0.03$), post hoc shown that the number of men participants was significantly higher than women participants in PASS group ($P<0.001$) (Table 4). All RTAC variables were significantly different between PASS and FAIL groups at 6-M after ACLR ($p<0.05$) except KOS-ADLS ($P=0.13$) (Table 4). Quadiceps strength deficits, poor functional performance on single-legged hop tests, and scoring lower on patient-reported outcome measures accounted for failing on RTAC. In addition, some participants complained of knee pain and knee effusion that prevented them from completing the single legged hop testing.

Table 4 Subjects' demographic and RTAC variables for f PASS and FAIL groups at 6-M after ACLR (Mean (SD)).

Variables	PASS	FAIL	P-value
Participants # (women/men)	48 (11/37)	47 (21/26)	0.03
Age (year)	25.75 (9.42)	29.43 (11.36)	0.133
BMI (N/m ²)	24.36(2.67)	25.38(4.39)	0.40
Graft type (Autograft/Allograft)	19/29	17/30	0.60
QI	103.33 (10.28)	91.72 (11.76)	<0.001
Single hop LSI	97.25 (5.15)	89.05 (11.97)	< 0.001
Cross-over hop LSI	97.96 (4.44)	93.85 (9.72)	0.008
Triple hop LSI	97.19 (4.40)	92.75 (7.35)	0.003
6-meter timed hop LSI	99.57 (5.39)	92.75 (8.58)	<0.001
KOS-ADLS	97.28 (2.53)	95.96 (4.36)	0.13
GRS	95.27 (4.04)	87.43 (11.67)	<0.001

3.7.1 Follow up at 12-M after ACLR

The rate of returning to participate in the same preinjury activity level at 12-M after ACLR among PASS and FAIL groups was 61.3% (Table 5). Thirty participants (81.1 %) of those who PASS RTAC at 6-M returned to participate in the same preinjury activity level at 12-M after ACLR, while 19 (44.2%) of those who FAIL the criteria at 6-M returned to participate in the same preinjury activity level at 12-M after ACLR (Table 5). The positive likelihood ratio of PASS group to return to the same preinjury activity level at 12-M after ACLR was 2.71, while the negative likelihood ratio of FAIL group to not return to the same preinjury activity level at 12-M after ACLR was 1.99 (p< 0.001).

Table 5 Return to participate in the same preinjury activity level 12-M after ACLR

	Returned at 12-M	Did not return at 12-M	Total
PASS	30	7	37
FAIL	19	24	43
Total	49	31	80

Table 6 Individual RTAC variables 6-M after ACLR prediction of returning to participate in the same preinjury activity level 12-M and 24-M after ACLR (R^2 : Nagelkerke R square).

	Return at 12-M after ACLR (R^2 (<i>p-value</i>))	Return at 24-M after ACLR (R^2 (<i>p-value</i>))
Classifying PASS V.s FAIL	0.173 (0.002)	0.154 (0.012)
Single hop LSI	0.102 (0.03)	0.308 (0.003)
Cross-over hop LSI	0.054 (0.09)	0.181 (0.011)
Triple hop LSI	0.088 (0.03)	0.212 (0.006)
6-meter timed hop LSI	0.201 (0.003)	0.313 (0.002)
KOS-ADLS	0.076 (0.04)	0.011 (0.497)
GRS	0.172 (0.009)	0.05 (0.183)

Classifying participants into PASS or FAIL on RTAC at 6-M after ACLR explained 17.3% of the variance for returning to participate in the same preinjury activity level 12-M after ACLR ($p=0.002$). At 6-M after ACLR, the single hop, triple hop, and 6-meter timed hop LSIs, KOS-ADLS, and GRS were significant predictors of returning to participate in the same preinjury activity level at 12-M after ACLR ($p<0.05$) (Table 6). The 6-meter timed hop LSI and GRS at 6-M after ACLR were the

strongest predictor variables, and they individually explained 20.1% ($p=0.003$) and 17.2% ($p=0.009$) respectively of the variance for returning to participate in the same preinjury activity level at 12-M after ACLR (Table 6). The combination of 6-meter timed hop LSI and GRS at 6-M explained 25.2% of the variance ($p=0.001$), however, only 6-meter timed hop LSI was a significant predictor of returning to participate in the same preinjury activity level at 12-M after ACLR (6-meter timed hop LSI: $p=0.029$; GRS: $p=0.064$) (Table7). When single hop LSI, triple hop LSI, and KOS-ADLS were added to the regression model, they explained only an additional 1.7% of the variance ($p=0.002$) and none of the variables were significant predictors ($p \geq 0.08$) (Table 7). The addition of each variable (single hop LSI, triple hop LSI, and KOS-ADLS) did not improve the predictability of the model significantly.

Table 7 Combination of RTAC variables 6-M after ACLR prediction of returning to participate in the preinjury activity level 12-M after ACLR (R^2 : Nagelkerke R square).

Model	Variable in the Model	12-M after ACLR(R^2)	Model (P value)	Step (P value)
Step 1	6-meter timed hop LSI	0.201	0.003	0.001
Step 2	6-meter timed Hop LSI, GRS	0.252	0.001	0.001
Step 3	6-meter timed Hop LSI, GRS, Single Hop LSI	0.261	0.002	0.56
Step 4	6-meter timed Hop LSI, GRS, Single Hop LSI, Triple Hop LSI	0.266	0.004	0.67
Step 5	6-meter timed Hop LSI, GRS, Single Hop LSI, Triple Hop LSI, KOS-ADLS	0.269	0.008	0.43

3.7.2 Follow up at 24-M after ACLR:

Complete data were available for 60 participants at 24-M follow-up testing after ACLR. Thirty-two participants (53.3%) of those who completed 24-M follow-up testing were classified as PASS on RTAC at 6-M after ACLR (Table 8). The rate of returning to participate in the same preinjury activity level among both PASS and FAIL groups at 24-M after ACLR was 66.7% (Table 8). Of those who PASS RTAC at 6-M after ACLR, 27 participants (84.4%) returned to participate in the same preinjury activity level 24-M after ACLR, and from those who FAIL on RTAC at 6-M after ACLR, 13 participants (46.4%) returned to participate in the same preinjury activity level 24-M after ACLR (Table 8). The positive likelihood ratio of PASS group to return to the same preinjury activity level at 24-M after ACLR was 2.70, while the negative likelihood ratio of FAIL group to not return to the same preinjury activity level at 12-M after ACLR was 2.31 ($p < 0.009$).

Table 8 Return to participate in the preinjury activity level 24-M after ACLR

	Returned at 24-M	Did not return at 24-M	Total
PASS	27	5	32
FAIL	13	15	28
Total	40	20	60

Classifying participants into PASS or FAIL on RTAC at 6-M after ACLR explained 15.4% of the variance of returning to participate in the same preinjury activity level 24-M after ACLR ($p=0.012$). At 6-M after ACLR, all of single-legged hop LSIs were significant predictors of return to participate in the same preinjury activity level at 24-M after ACLR (Table 6). Six-meter timed hop and single hop LSIs were the strongest

predictor variables, and they individually predicted 31.3% ($p=0.002$) and 30.8% ($p=0.003$) respectively of the variance of returning to participate in the same preinjury activity level 24-M after ACLR. The combination of 6-meter timed hop and single hop LSIs 6-M after ACLR explained 36.1% of the variance ($p < 0.001$), however, neither 6-meter timed hop nor single hop LSIs were significant predictors (6-meter timed hop LSI: $p=0.108$; single hop LSI: $p= 0.074$) (Table 9). Adding triple hop and cross-over LSIs to the regression model did not improve the predictability of model significantly as they explained only an additional 1.8% of the variance of returning to participate in the same preinjury activity level at 24-M after ACLR with none of the variables significant predictors ($p>0.05$) (Table 9).

Table 9 Combination of return to activity criteria 6-M prediction return to the preinjury activity level 24-M after ACLR (R^2 : Nagelkerke R square).

Model	Variable in the Model	24-M after ACLR (R^2)	Model (P value)	Step (p value)
Step 1	6-meter timed Hop LSI	0.313	0.002	<0.001
Step 2	6-meter timed Hop LSI, Single Hop LSI	0.361	< 0.001	< 0.001
Step 3	6-meter timed Hop LSI, Single Hop LSI, Triple Hop LSI	0.362	0.001	0.92
Step 4	6-meter timed Hop LSI, Single Hop LSI, Triple Hop LSI, Cross-over Hop LSI	0.379	0.002	0.34

3.8 Discussion

The purpose of this study was to determine whether RTAC variables conducted at 6-M after ACLR can predict return to participate in the same preinjury activity level 12-M and 24-M after ACLR, and to determine which individual or a

combination of RTAC variables at 6-M after ACLR predicts return to participate in the same preinjury activity levels 12-M and 24-M after ACLR. The results of this study reveal that RTAC variables, individually or combined, can predict return to participate in the same preinjury activity levels at both 12-M and 24-M after ACLR. In addition, those participants who demonstrated normal knee function and limb-to-limb movement symmetry during functional tasks at 6-M after ACLR are more likely to return to participate in their preinjury activity level 12-M and 24-M after ACLR.

Though the rates of returning to participate in the same preinjury activity level 12-M and 24-M after ACLR among all participants were within similar ranges reported by other`s ^{113,120}. The rate of returning to participate in the same preinjury activity level for those who were classified as PASS at both 12-M and 24-M after ACLR was superior compared with other studies due to the use of strict RTAC that emphasize normal knee function and limb-to-limb movement symmetry. Furthermore, those participants who returned to participate in the same preinjury activity level at both 12-M and 24-M after ACLR were almost three times more likely to PASS RTAC 6-M after ACLR than those who did not return. While those who did not return to participate in the same preinjury activity level 12-M and 24-M after ACLR were at or over two times more likely to FAIL respectively 6-M after ACLR than those who did return. Participants in PASS group had normal quadriceps strength and symmetrical limb-to-limb movement during dynamic functional activities, not favoring one of their lower limbs, which potentially make them capable of participating in high level activities. In addition, these participants are more likely not to overuse either one of their lower extremities during highly demanding activities. In result, PASS participants most probably place themselves at lower risk for future knee injuries or knee pathologies. A Recent systemic review and meta-analysis study reports that return to preinjury activity level was favored in athletes with Symmetrical hopping performance and in athletes who participate in running, cutting, decelerating and

pivoting activities⁶⁸.

Single-legged hop tests, which are performance-based tests used for assessing patient's muscle strength, power, neuromuscular control, and tolerance for loading the knee joint, can predict returning to participate in the same preinjury activity level 12-M and 24-M after ACLR¹²¹. The findings of this study reveal that the combination of 6-meter timed hop LSI and GRS at 6-M after ACLR was the best predictor for returning to participate in the same preinjury activity levels 12-M after ACLR and the combination of 6-meter timed hop and single hop LSIs at 6-M after ACLR was the best predictor for returning to participate in the same preinjury activity level 24-M after ACLR. In addition, single-legged hop tests explain a larger portion of the variance of returning to participate in the same preinjury activity levels at 24-M when compared to 12-M after ACLR. This finding was not surprising as athletes returning to Level I or II sporting activities need to perform movement-specific tasks involve take-off and landing maneuvers that single-legged hop tests replicate. Single-legged hop tests can predict patient-reported knee function after ACLR³⁴ and have the potential to discriminate between those athletes who can return to their previous activity level and who cannot return after ACLR^{9,111}. Clinically, single-legged hop tests also can detect limb-to-limb performance deficits which can assist clinicians in modifying the rehabilitation program by integrating more agility and plyometric training in attempt to reduce limb-to-limb movement asymmetry^{122,123}. In this study, 6-meter timed hop LSI was the strongest significant predictor of return to the same preinjury activity level at both 12-M and 24-M after ACLR. While this study does not provide an explanation as to why the 6-meter timed hop was the strongest predictor for the two time points, it could be hypothesized that it might be easier for participants to perform a series of consecutive hops over 6-meter distance as fast as they can without changing in direction, having a controlled landing, or stopping their body momentum. In contrast, distance hops may challenge patients to a greater extent as they are instructed to hop for distance, and stop their body momentum from moving forward and

maintain their body balance during landing.

Of the patient-reported measures, GRS was the single significant predictor for returning to the same preinjury activity level 12-M after ACLR while none of patient-reported measures was significant predictor for returning to preinjury activity level at 24-M after ACLR. GRS is a single question that assesses participants' perception about their current global knee function during sports activities after ACLR. While GRS scores can vary between participants as some athletes may not be fully confident about their knee function 12-M after ACLR, this effect diminishes 24-M after ACLR as participants are more likely to become more confident with their knee function. Therefore, participants might require highly functional skills to succeed while participating in their activities after ACLR.

The results of this study suggest the use of a combination of performance-based and patient-reported knee function measures as RTAC for clearing patients to return to participate in the same preinjury activities. RTAC have significant implications on the clinical management of patients after ACLR and on clinical decision making as clinicians can use these criteria as tools to identify those patients who achieved symmetrical limb-to-limb movement during functional activities and who are satisfied about their knee functional performance during activity of daily livings. Additionally, clinicians can determine which patients are most likely to return to participate in the same preinjury activity level 12-M and 24-M after ACLR based on their performance on RTAC. The result of this study support similar findings reported in previous studies. Fitzgerald et al ⁹ reported that a battery of functional tests and questionnaires outcome measures, similar to the RTAC variables, has the potential to differentiate between those patients with poor dynamic knee stability from those patients with good knee dynamic stability early after ACL injury. Additionally, Fitzgerald et al ⁹ reported that these same measures can predict returning to previous activity level in the short term in patients who were treated non-operatively. The findings of this study and Fitzgerald ⁹ suggest that using performance-based and

patient-reported measures might be the ideal way for assessing subject's return to activity readiness after ACL rupture or ACLR.

The results of this study also highlight the importance of using performance-based and patient-reported measures to identify participants with poor knee function and limb-to-limb movement asymmetry before clearing them to return to high demanding activities. Many athletes after ACLR continue to exhibit residual impairments including quadriceps strength deficits, poor knee function, and asymmetrical limb movement by relying more on the uninvolved limb during dynamic functional activities which may be susceptible to deteriorating long-term knee joint health ^{7,23-25,27}. Therefore, using return to activity criteria as a key tool to identify these participants early before they begin participating in high demanding activities and provide them with an additional sessions of intensive rehabilitation program to improve their knee function performance and movement symmetry. Participants who do not improve their knee functional performance and limb-to-limb movement symmetry, they might need to be instructed to modify their activity level to a lower level. Additionally, these participants should avoid risky multidirectional activities as they may put them at increased risk of reinjury or poor long term joint health. Further research might evaluate the incidence of reinjury and the development of osteoarthritis among participants who fail the return to activity criteria.

The combination of 6-meter timed hop LSI and GRS and the combination of 6-m timed hop and single hop LSIs at 6-M after ACLR can predict only one fourth and one third of the variance of returning to participate in the same preinjury activity levels 12-M and 24-M respectively after ACLR. However, the RTAC criteria used in this study was originally instituted to assess athlete's knee functional performance

during basic functional tasks and to frame safe guidelines to clear athletes to begin participating gradually in their preinjury activities. In addition, single-legged hop tests are cost efficient method to assist lower extremity functionality after knee injury or surgery and are simple to be conducted in a clinical sitting. The results of this study suggest that additional measures may predict returning to the same preinjury activity level 12-M and 24-M after ACLR such as changes in life style, scholastic transition, lower opportunity to participate in activities, or socioeconomic status ⁸⁵. Other factors related to fear of reinjury may explain why some subjects have not returned to the same preinjury activity level. Studies have reported that some patients whose physical or functional impairments have resolved may choose not to return to sport activities due to psychologically unready for return to sport activities ^{120,112,124,125}.

3.9 Limitation

In this study we investigated which variables were predictive of returning to the same preinjury activity level 12-M and 24-M after ACLR using only those participants who participated in level I/II activities and who underwent ACLR. Therefore we cannot generalize the findings of this study to those participants who participate in less demanding activities levels (level III/ VI) and to those patients with ACL rupture and chose to be managed non-operatively. In addition, there was a group of participants who passed return to activity criteria earlier after ACLR. However, in this study we used 6-M after ACLR as baseline testing for predicting return to the same preinjury activity level 12-M and 24-M after ACLR instead of using the exact date of passing return to activity criteria. However, in this study 6-M after ACLR was chosen because most athletes are typically cleared to begin participating in their

preinjury activities around that time ¹²⁶. Furthermore, in this study we used a patient-reported variable related to activities of daily living, KOS-ADLS, instead of using variables related to sport activities to predict returning to preinjury activity level. The use of the KOS-ADLS indicated that participants were able to perform their activities of daily living unrestricted, therefore ensuring participants' readiness to be cleared to return to their preinjury activity level. Further research needed to investigate return to the same preinjury activity level using outcome measures related to participation in sport activities.

3.10 Conclusion

In conclusion, participants who returned to the same preinjury activity level 12-M and 24-M after ACLR are more likely to demonstrate normal limb-to-limb symmetry and report high global knee function at 6-M after ACLR. While those who didn't return are more likely to exhibit limb asymmetry and poor knee function which might create barriers for returning to preinjury activity level. Additionally, implementing return to activity criteria into clinical rehabilitation setting is the best available method to determine subject's readiness to return to their preinjury activities after ACLR.

**NO DIFFERENCE BETWEEN MANUAL AND MECHANICAL
PERTURBATION TRAINING ON THE KNEE BIOMECHANICS AND
FUNCTIONAL PERFORMANCE AFTER ACL RUPTURE**

4.1 Abstract

Manual perturbation training is a type of neuromuscular training that improves knee functional performance and gait mechanics in patients with ACL rupture. However, it is not widely used in the rehabilitations clinics, and requires extensive physical labor and time from the treating therapist. Administering perturbation training using mechanical device requires less demand from the treating therapist. However, it is unknown whether administering perturbation training using mechanical device provides effects similar to manual perturbation on knee mechanics and functional performance of patients with an acute ACL rupture.

Purpose: To investigate whether administration of perturbation training using mechanical device provides effects similar to manual perturbation training on knee kinematic and kinetic, performance-based, and patient-reported measures in patients with ACL rupture.

Materials: Eighteen level I or II subjects with acute ACL rupture participated in this study. Nine subjects received mechanical perturbation training (3DOF group) and 9 subjects matched by sex and age received manual perturbation training (manual group). Patients completed pre and post-training testing that include 3-D gait motion analysis (kinematic and kinetic) and functional testing. The functional testing included performance-based tests (isometric quadriceps strength and four single-legged hop tests) and two patient-reported measures (Knee Outcome Survey-Activities of Daily

Living Scale (KOS-ADLS) and the Global Rating Score of perceived knee function (GRS)). Minimal clinically important differences (MCID) were used for sagittal plane knee joint kinematics and kinetics between limbs (knee excursion angle: $\geq 3^\circ$, external knee moments: $\geq 0.04 \text{ Nm/kg}\cdot\text{m}$)

Results: There was no significant group by time by limb interaction for all knee kinematic and kinetic variables ($p > 0.3$). A significant limb by time interaction was found for knee flexion excursion during WA ($p = 0.012$) with the involved limb demonstrated significantly lower excursion before training and increased significantly after training ($p \leq 0.033$). Main effect of limb was found for knee flexion excursion during midstance and for external knee extension moment with the involved limb demonstrated lower knee excursion and moment. There was a significant main effect of time for external knee flexion moment ($p = 0.022$) with subjects in both groups improved their external knee flexion moment. Both groups demonstrated limb-to-limb differences that exceeded MCID for knee excursion during MS and external knee extension moments at pre-training testing. 3DOF group had limb-to-limb differences that exceeded MCID for external knee flexion moment at pre-training testing. After training, only 3DOF group's limb-to-limb differences did not exceed MCID for knee excursion during MS. Additionally, 3DOF group achieved improvement that exceeded MCID for external knee flexion moment after training.

There was no significant time by group interaction for performance-based and patient-reported functional measures ($p \geq 0.2$). There was significant main effect of group for all single-legged hops LSIs ($p \leq 0.03$) with the 3DOF group demonstrated higher hopping performance. There was also significant main effect of time for single hop,

($p=0.013$), triple hop ($p=0.023$) and 6-meter timed hop ($p=0.007$) LSIs, and KOS-ADLS ($p<0.043$).

Discussion: Mechanical perturbation training provides effects similar to manual perturbation training on knee kinematic and kinetic, knee functional performance, and patient-reported measures of patients with an acute ACL rupture. Additionally, mechanical and manual perturbation training were effective in improving patients' functional performance. Patients continued to demonstrate limb-to-limb kinematic and kinetic asymmetry after training regardless of treatment group.

4.2 Introduction

The anterior cruciate ligament (ACL) is the most common injured ligament in the knee joint, with approximately 250,000 ACL injuries occur annually in the United States¹. The repeated episodes of knee instability is a common complaint of patients with ACL rupture⁸⁷. The occurrence of repeated episodes of knee instability may result in significant impairments that challenges patients' ability to perform both daily living and sport activities^{26,127-129}. Joint effusion, range of motion deficits, quadriceps strength deficits, neuromuscular dysfunction, and aberrant gait pattern are common after ACL injury^{6,20,43}. These functional limitations and aberrant gait pattern may continue to persist for long periods after the injury and after reconstruction surgery¹³⁰. The presence of functional limitations and aberrant gait patterns may lead to negative consequences on the patients' functional performance⁴⁹. Paterno and colleagues found that abnormal kinematic and kinetics during drop jumping can account for the prediction of secondary ACL injury¹⁰⁷. Additionally, it has been suggested that aberrant gait patterns may associate with the development of knee osteoarthritis¹³¹⁻¹³³. Success after ACL rupture relies on the resolutions of knee functional limitations and

aberrant gait pattern. Additionally, the outcomes after reconstruction surgery is linked to the status of the knee functional performance and quadriceps strength level prior to surgery^{33,134}. Currently, ACL rehabilitation programs emphasize early resolution of knee impairments and functional limitations to accelerate the functional recovery and facilitate a safe and successful return to participation in both daily living and sport activities⁶⁵. It has been reported that, those patients who resolve their knee impairments and quadriceps strength deficit prior to reconstruction surgery are more likely to have better knee functional outcomes after surgery^{134,135}.

While the current standards of care for young athletes with ACL rupture is early ACL reconstruction (ACLR). Considering the condition of the knee joint might be of more important than the time course from the injury^{28,32}. Previous studies reported that operating on patients with knee impairments and functional limitations associated with poor outcomes post-surgically^{31,32,130}. Additionally, early ACLR shows no benefits over optional delayed reconstruction or non-surgical management at all with more than 50% of athletes continued non-surgical management with no increase in adverse events¹³⁶. Additionally, long-term follow-up studies revealed that the incident of knee osteoarthritis was not different between surgical and non-surgical management^{109,137}. There are certain instances that need to be considered in the process of decision making regarding the management options. This includes the time to surgery and the recovery time from surgery for athletes who sustain a pre-season or early season ACL rupture and for construction workers during seasonal laborers who wish to postpone ACLR until after the busy work season. Therefore, the non-surgical management becomes a viable option for athletes who plan to delay the ACLR surgery in the short or long term. The effectiveness of pre-surgical¹⁰⁶, delayed-surgery¹³⁸, and

non-surgical⁵ rehabilitation is clearly supported. Additionally, patients who resolve functional deficits before surgery have a better chance to demonstrate good knee function after reconstruction surgery^{33,134}.

To this end, the current treatment algorithm for patients with an ACL rupture who plan to delay surgical intervention in the short or long term is to participate in strength training augmented with perturbation training program^{52,53}. Perturbation training is a type of neuromuscular training that mitigates abnormal movement pattern and improve the dynamic knee stability and function^{5,15,51}. Multiple studies investigating the effect of the manual perturbation training after ACL injury found that administration of manual perturbation training is an effective intervention that promotes dynamic knee stability⁵¹, enhances dynamic knee function, normalizes knee movement patterns^{11,15}. Furthermore, manual perturbation training increases the likelihood and success rate for highly active individuals to return to short term sport activities without ligament reconstruction⁵. The perturbation training, however, is not widely used as part of the ACL rehabilitation program in the United States. Further, the perturbation training is administered manually which requires an extensive one-on-one time from the treating therapist⁵⁴. The effect of administering perturbation training using mechanical device as part of the ACL rehabilitation program has not been investigated. Administering perturbation training using mechanical device facilitates the use of the training in a wide range of rehabilitation settings. Additionally, it also allows administration of controlled and standardized perturbation stimuli with an attempt to optimize the ACL rehabilitation programs.

Simbex LLC has developed an automated device, called Reactive Agility System, which provides mechanical perturbations based on controls and settings that

are set by a physical therapist. This device has a moveable plate embedded in a platform that provides complex translations in different directions in the horizontal plane (three degrees of freedom (3DOF) plate). Mechanical perturbation devices have been widely used in rehabilitation programs for patients with different neurological and musculoskeletal impairments^{55,59,60,139–141}. Mechanical perturbation has been advocated to be an effective training intervention by re-educating the proprioceptive system, improving mechanoreceptor function, and restoring normal neuromuscular coordination by exposing the patients to controlled and progressive perturbing stimuli^{55–57}. Furthermore, mechanical perturbation has the potential to improve the balance abilities⁵⁵, increase postural reflex by reducing reaction time⁵⁸, improve balance and stability in patients with OA⁵⁹, and enhance the timing and pattern of muscle activation⁶⁰. The aim of this study was to evaluate whether administration of 10-training sessions of mechanical perturbation using 3DOF plate provides effects similar to 10-training sessions of manual perturbation on gait mechanics, functional performance-based and patient-reported measures in patients with ACL rupture.

4.3 Methods

Eleven subjects with an acute isolated unilateral ACL rupture (<7 months) between the ages 14-55 (mean age: 21.32±5.52) were enrolled into this pilot study. All subjects were regular participants in level I or II activities that include jumping cutting, pivoting, and lateral movements (i.e. soccer, football, rugby, tennis, ice hockey, and wrestling) for at least 50 hours per year prior to their ACL injury⁷. Subjects were excluded from the study if they had more than one prior ACLR in the ipsilateral or contralateral limb, previous serious lower extremities injury (i.e. fracture), concurrent multiple ligamentous injury, repairable meniscus, osteochondral

defect ($>1 \text{ cm}^2$), or demonstrated less than a 3 mm side to side difference in passive anterior knee laxity measured with a KT-2000 arthrometer⁸⁹. The ACL injury and concomitant knee injury were determined using both physical examination and magnetic resonance imaging (MRI). Subjects in this study were primarily recruited through the University of Delaware Physical Therapy Clinic. The study was approved by the University of Delaware's Institutional Human Subjects Review Board. All subjects provided written informed consent for participation in this study.

Subjects were assigned to receive perturbation training using mechanical device "Simbex device". The mechanical device has an embedded plate that provides translations in three degree of freedom (3DOF group) (Figure 14). The subjects in 3DOF group received 10-training sessions of perturbation training using the "Reactive Agility System" device developed by Simbex LLC (Lebanon, NH) (Figure 15). The Reactive Agility System has an embedded moveable plate that provides standardized mechanical perturbations. The 3DOF mechanical perturbation protocol involved multidirectional translations in X and Y directions with optional rotation up to 10° around the Z axis in the horizontal plane. The 3DOF mechanical perturbation training stimuli were executed in various combinations: eight directions, three amplitudes, three velocities, and two rotational directions (Figure 16).

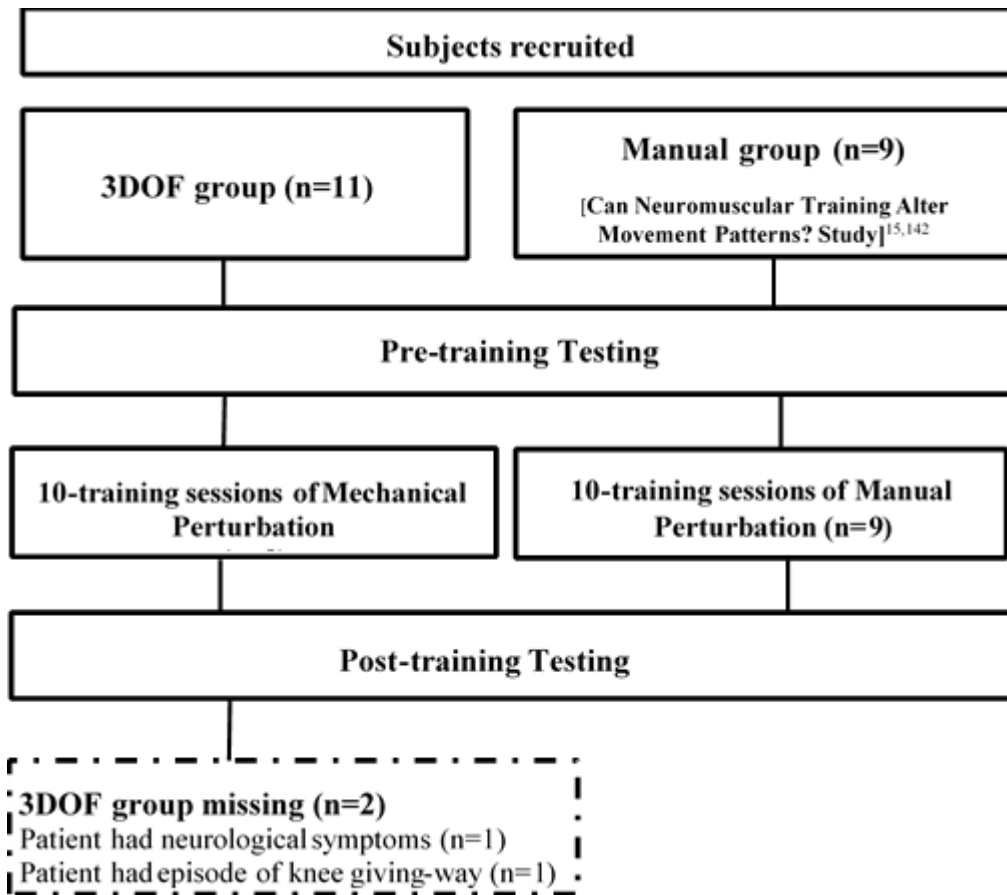


Figure 14 Subject's participation in the study

The maximum velocity and acceleration limits of the 3DOF plate during planar translation are 400mm/ sec and 25000 mm/sec² and the rotational translation was 120°/sec and 10000°/sec² respectively. The 3DOF plate allows three translational amplitudes: short: 22mm, medium: 33mm, and long: 45mm; and three planar velocities; low: 75mm/sec, medium: 150mm/sec, high: 250mm/sec.

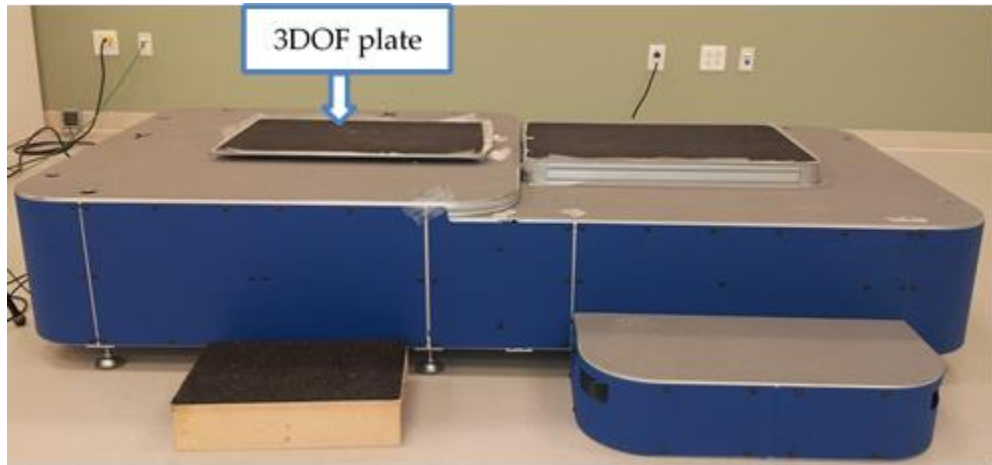


Figure 15 Reactive Agility System” mechanical perturbation

The parameters (direction, amplitude, velocity, and acceleration, and deceleration) of the 3DOF mechanical perturbation are similar to the manual perturbation training previously described by Fitzgerald⁵ and were determined using marker velocity and displacement in our motion analysis laboratory. The complete 3DOF perturbation training protocol is outlined in Appendix A. Nine subjects of the 3DOF group completed the 10-training sessions of mechanical perturbation and both the pre and post-training testing sessions. Two subjects of the 3DOF group did not complete the study. One subject had neurological symptoms before completing the motion analysis testing at the pre-training testing. The second subject had an episode of knee giving-way outside the training program that caused gross knee effusion and ACL reconstruction surgery was scheduled soon afterward which did not allow us to complete the rest of the training sessions (Figure 14).

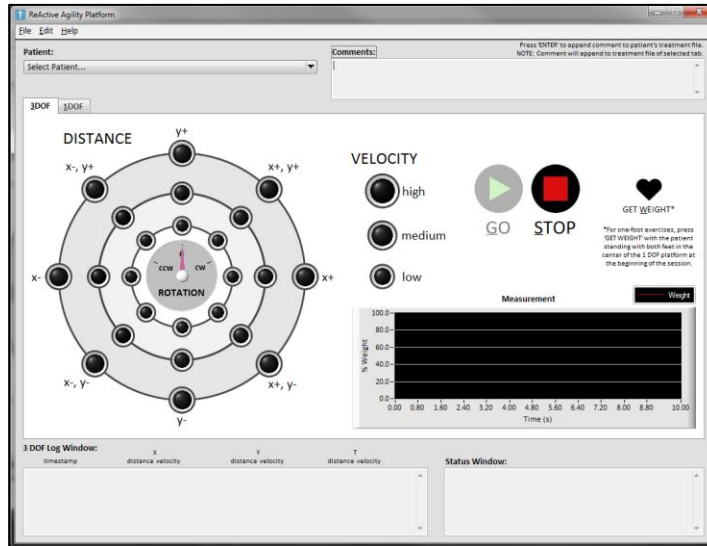


Figure 16 The 3DOF control panel interface

In addition to the subjects in 3DOF group, 9 subjects from a previous study entitled “Can Neuromuscular Training Alter Movement Patterns? Study” matched by age and sex were used to serve as a comparison group (Manual group^{15,142}). All subjects in the previous study received 10-training sessions of perturbation training administered by a physical therapist. Manual perturbation training program included administration of purposeful manipulation of support surfaces including rockerboard, rollerboard, and rollerboard and platform by a physical therapist. The manual perturbation training was previously described by Fitzgerald et al⁵. One difference between the mechanical and manual perturbation training is that the manual perturbation training protocol included the rockerboard technique which was not part of the 3DOF mechanical perturbation training program.

After each perturbation training session, five subjects from the 3DOF group who planned to pursue a long term non-surgical management received agility drill training.

All subjects in the manual group were scheduled for reconstruction surgery and did not receive agility training. Agility drill training was administered at the end of each training session with all subjects wearing knee functional brace. Agility drill training was administered to improve subjects' lower extremities muscles neuromuscular coordination and to increase patients' ability to quickly change running directions⁹⁷. Agility training was administered for patients if they reported no episode of knee instability or "giving way" since the ACL injury. Agility training was initiated once patients achieved full knee range of motion (ROM), minimum effusion, and pain-free with loading activities. Agility techniques included forward and backward running with quick start and stop, side shuffling, carioca, figure-eight running, and 45-degree cutting and sprinting, and 90 degrees cutting maneuvers. Subjects began performing agility training at 35% to 50% of their perceived maximum effort and were progressed to full-effort training over the 10-training sessions. Perturbation training (mechanical or manual) and agility training were progressed based on the subject's tolerance for activity and if they reported no joint pain, soreness, or development of joint effusion. Sport-specific tasks (basketball dribbling, ball throwing, ball kicking) were also integrated into the perturbation training (mechanical and manual) when the subjects demonstrated minimal balance disturbance and minimal co-contraction responses during perturbation training and tolerance to full-effort agility training without pain or swelling⁹⁷. In addition, subjects in both groups with $QI < 80\%$ received a supervised, progressive strengthening training augmented with neuromuscular electrical stimulation (NMES) to improve quadriceps strength. Subjects with $80 \leq QI < 90\%$ received a supervised progressive strengthening training without NMES. Subjects with

QI \geq 90% were instructed to start a fitness strengthening program to improve their quadriceps strength²⁴.

4.4 Testing

Subjects completed a pre and post-training testing sessions that included both clinical and motion analysis testing. The pre-training testing was administered once subjects demonstrated no knee pain, minimal knee joint effusion as measured with the modified stroke test¹⁰⁰, exhibit full knee joint range of motion, and demonstrate \geq 70% quadriceps index between limbs. The pre and post-training testing consist of performance-based tests (quadriceps strength test and single-legged hop tests⁹⁹), patient-reported questionnaires (Knee Outcome Survey- Activities of Daily Living Scale (KOS-ADLS) and Global Rating Score (GRS)), and gait motion analysis testing within two weeks of the initiation of the training protocol (Pre-training) and within two weeks after the completion of 10-training sessions (Post-training) (Figure 14).

4.4.1 Performance-based testing

Quadriceps strength was measured during a maximal voluntary isometric contraction (MVIC) using the burst superimposition technique on an electromechanical dynamometer (Kin-Com, Chattanooga Corp, Chattanooga, TN)⁹⁸. Subjects were seated with their hip and knee flexed to 90° with stabilization at the hip, knee, and ankle. Subjects performed three practice trials (two sub-maximal and one maximal effort) before each measured trial. Upon testing, subjects were instructed to maximally contract their quadriceps muscles. Quadriceps muscle force output was measured and recorded using custom-written software (LabVIEW, National Instruments, Austin, TX) with a 200-Hz sampling rate. The quadriceps strength test

was performed with a maximum of 3 trials per limb. To avoid the influence of fatigue, subjects were given 1-2 minutes of rest between trials. The test was first performed on the uninvolved limb followed by the involved limb. Quadriceps index (QI) was calculated by dividing the involved limb's quadriceps force by the uninvolved limb's quadriceps force multiplied by 100.

Single-legged hop testing was measured using four single-legged hop tests: single hop, cross-over hop, and triple hop for distance, and 6-meter timed hop⁹⁹. A 6-meter measuring tape affixed to the floor with two additional pieces of tape 7.5 centimeters on either side of the tape. Hop tests for distance were measured with the patient standing on one limb. Subjects started all hopping tests by lining their feet before the measuring tape. All distances were measured from the final position of the subject's heel after landing. Subjects were permitted to perform the hop tests once they demonstrate symmetrical knee range of motion, minimal knee joint effusion¹⁰⁰, $QI \geq 70\%$, and no complaints of pain with in-place hopping. For the single hop, the subject hops forward one time as far as possible. For the cross-over hop, the subject hops forward three consecutive times as far as possible, each time crossing over the outer parallel lines. For the triple hop, the subject hops forward three consecutive times as far as possible. For the 6-meter timed hop, the subject hops as quickly down the 6 meter course as fast as possible. All subjects performed two practice trials followed by two measured trials of each hop test on both limbs. The uninvolved limb was tested first then followed by the involved limb. Measured trials were counted when subjects landed on the same foot and demonstrated body balance during landing phase without touching the ground with the other foot. Limb symmetry indexes (LSIs) for hop tests was calculated. Hop performance for distance was calculated as the

percentage of the average involved limb hop distances divided by the average uninvolved limb hop distances for each individual hop test for distance multiplied by 100. In the 6-meter timed hop, LSI was calculated as the percentage of the average uninvolved limb hop divided by the average involved limb hop multiplied by 100.

4.4.2 Patient-reported measures

After all performance-based testing were completed, subjects filled out patient-reported questionnaires including KOS-ADLS and GRS. The KOS-ADLS and GRS were administered after the completion of the performance based tests to allow subjects to better rate their knee functional status. The KOS-ADLS is a patient-reported measure consisting of 14-items regarding the subjects' perception of their knee symptoms and functional limitations and how these limitations affect their ability to perform activities of daily living such as walking, ascending and descending stairs, kneeling, sitting, and squatting¹⁰¹. The KOS-ADLS has been shown to be a reliable, valid, and responsive measure for assessing functional limitations of the knee, with high intraclass coefficients of 0.97 and test-retest reliability¹⁰². Scores for the KOS-ADLS are reported as a percentage of the subject's points divided by the total possible points multiplied by 100. The GRS will be used to assess subjects' current knee functional performance. The GRS is a one-item question that asks subjects to rate their current knee function on a scale from 0% to 100%, with 0% being the inability to perform any activity and 100% being their level of knee function prior to injury, including sports activities. It has been reported that analogue GRS has a high test-retest intraclass coefficients of 0.96¹⁰³.

4.4.3 Motion analysis testing

Gait kinematic and kinetic data were captured using a passive 8-camera, 3-dimensional motion analysis system (VICON, Oxford Metrics Ltd, London, United Kingdom) at a 120Hz frequency rate. Twenty static retro-reflective markers were placed on the anatomic landmarks of the foot, ankle, shank, thighs, and pelvis of each patient to determine joint centers and segment position. Rigid shell clusters were secured to the pelvis and distal-lateral aspects of the shanks and thighs to track segment motion during gait. An embedded 6-component force plate (Bertec Corp, Worthington, Ohio) was simultaneously collecting kinetic data at 1080 Hz frequency rate during the gait cycle. Eight walking trials were collected for each limb while the patients maintained a self-selected walking speed with $\pm 5\%$ variability. Data from five good walking trials were post-processed using rigid body analysis and inverse dynamics with custom software programming (Visual3D, C-Motion, Inc., Germantown, MD, USA; LabVIEW 8.2, National Instruments Corp, Austin, TX, USA). Kinematic and kinetic data were low pass filtered at 6 Hz and 40 Hz respectively. Heel strike contact (HS) and toe off (TO) gait events were determined using a 50 Newton force plate threshold. Walking trials were normalized to 100% of stance phase and then averaged for statistical analysis. Knee excursions were computed during weight acceptance (WA) interval (from heel strike (HS) to peak knee flexion (PKF)) and for mid-stance (MS) from PKF to peak knee extension (PKE). External knee moments were computed for the knee joint at PKF for external knee flexion moment and at PKE for external knee extension moment.

4.5 Return to Activity Criteria

At pre and post-training testing sessions, a battery of return to activity criteria (RTAC) that involved performance-based (QI and all four single-legged tests and patient-reported measures (KOS-ADLS and GRS) were used to determine patients' readiness to return to preinjury activity level. Subjects who achieved at least 90% on all RTAC variables were classified as PASS and those who failed to achieve 90% on any of the RTAC variables were classified as FAIL. At post-training testing, subjects who passed the RTAC were instructed to begin gradually participating in the preinjury activity level. While those who failed on the RTAC variables were instructed to continue the training program on their own for 3-6 months.

4.6 Statistics

Independent t-test was used to determine whether there were differences between groups (3DOF and Manual) for subjects' demographics, performance-based, patient-reported, and biomechanical measures at pre-training testing session. Paired t-test was also used to determine whether there were significant differences between the involved and uninvolved limbs for the biomechanical measures of the manual and 3DOF groups. A 2x2x2 analysis of variance (ANOVA) was used to evaluate differences between treatment groups (between-subjects factor: 3DOF and Manual), over time (within-subjects factor: pre-training and post-training), and between limbs (within-subjects factor: involved and uninvolved limbs) for the biomechanical measures. A 2x2 analysis of variance (ANOVA) was used to evaluate differences between treatment groups (between-subjects factor: 3DOF and Manual), over time (within-subjects factor: pre-training and post-training) for performance-based and patient-reported measures. Independent t-test was used as post hoc tests to determine

whether significant differences existed between 3DOF or Manual groups at pre and post-training testing sessions for the performance-based, patient-reported measures, and biomechanical measures. Paired t-tests were used as post hoc tests to determine whether 3DOF or Manual groups demonstrated significant improvement between pre and post-training testing sessions for the performance-based, patient-reported measures, and biomechanical measures. Paired t-tests were also used to determine whether significant differences between the involved and involved limbs exist for biomechanical variables at pre and post-training testing sessions for the biomechanical measures. Minimal clinically important differences (MCID) were used for sagittal plane knee joint kinematics and kinetics. These MCID's have been established to determine if differences between limbs are clinically meaningful (knee excursion angle: $\geq 3^\circ$, external knee moments: $\geq 0.04 \text{ Nm/kg}\cdot\text{m}$)¹⁵. In this study we also used the MCID for knee kinematics and kinetic to determine if patients demonstrated clinically meaningful changes between the pre and post-training testing sessions.

4.7 Results

Nine subjects from the 3DOF group and 9 matched subjects by sex and age from a previous study (manual group) completed a pre and post-training testing and 10-training sessions of perturbation training. There was no difference in women to men ratio, age, and time from injury to the pre-training testing session between 3DOF and manual groups ($P \geq 0.233$). The BMI, however, was significantly different between groups with manual group demonstrating larger BMI compared to the 3DOF group ($p=0.044$) (Table 10).

Walking velocity during motion analysis testing was not different between 3DOF and manual groups ($p=0.576$). There was no significant group by time by limb

interaction for all knee kinematic and kinetic variables ($p>0.3$) (Table 11). There was a significant limb by time interaction for knee excursion during WA ($p=0.012$). Post hoc test revealed that significant difference existed between limbs for knee excursion during WA at pre-training testing session (involved limb: 17.18 ± 4.37 ; uninvolved limb: 19.60 ± 4.32 ; $p=0.001$). Post hoc test revealed also that the involved limb increased knee excursion during WA significantly after training ($p=0.033$) (Figure 17).

Table 10 Subjects demographic of manual and 3DOF groups at pre-training testing of the 3DOF and manual groups (Mean (SD)).

Variables	3DOF group (n=9)	Manual group (n=9)	P-value
Subjects #(women/men)	9 (2/7)	9 (2/7)	0.712
Age (year)	21.32 (5.52)	22.23 (5.54)	0.731
BMI (kg/m ²)	24.13 (3.67)	28.17 (4.15)	0.044
Time from injury to pre-testing session (month)	1.93 (1.39)	1.13 (1.37)	0.233
Walking velocity	1.56 (0.14)	1.53 (0.13)	0.576

Table 11 Knee kinematic and kinetic of the manual and 3DOF groups at pre and post-training testing (Mean (SD))

Variable	Pre-Training Testing				Post-Training Resting				Group *Time*Limb
	Manual involved (n=9)	Manual Uninvolved (n=9)	3DOF Involved (n=9)	3DOF Uninvolved (n=9)	Manual involved (n=9)	Manual Uninvolved (n=9)	3DOF Involved (n=9)	3DOF Uninvolved (n=9)	
Knee excursion WA (°)	18.74 (5.56)	20.77 (4.79)	15.63 (2.70)	18.44 (3.79)	19.37 (5.48)	20.32 (4.31)	17.54 (3.97)	17.99 (4.33)	0.31
Knee excursion MS (°)	18.56 (7.57)	25.17 (8.34)	14.62 (5.15)	19.72 (6.77)	19.71 (7.61)	22.75 (6.99)	17.09 (5.90)	19.98 (6.51)	0.525
EKFM (Nm/kg*m)	0.385 (0.12)	0.41 (0.12)	0.47 (0.16)	0.54 (0.13)	0.42 (0.14)	0.43 (0.15)	0.52 (0.17)	0.56 (0.130)	0.746
EKEM (Nm/kg*m)	0.124 (0.16)	0.22 (0.12)	0.057 (0.11)	0.14 (0.086)	0.12 (0.16)	0.22 (0.13)	0.087 (0.06)	0.15 (0.098)	0.475

EKFM: External knee flexion moment; EKEM: External knee extension moment

There was significant main effect of limb for knee excursion during MS ($p=0.001$) and for external knee extension moment ($p=0.008$) with the uninjured limbs demonstrated larger knee excursion and external knee moment. There was main effect of group for external knee flexion moment ($p=0.022$) with the 3DOF group demonstrated higher external knee flexion moment. Significant main effect of time was found for external knee flexion moment ($p=0.022$) with subjects in both groups improved their external knee flexion moment after training (Table 11)

Both groups demonstrated clinically meaningful limb-to-limb differences that exceeded the MCID for knee excursion during MS and for external knee extension moments at pre-training testing. 3DOF group also demonstrated clinically meaningful limb-to-limb differences that exceeded the MCID for external knee flexion moment at pre-training testing. After training, limb-to-limb differences of 3DOF group did not exceed MCID for knee excursion during MS. Additionally; 3DOF group achieved clinically meaningful limb-to-limb improvement that exceeded the MCID for external knee flexion moment after training.

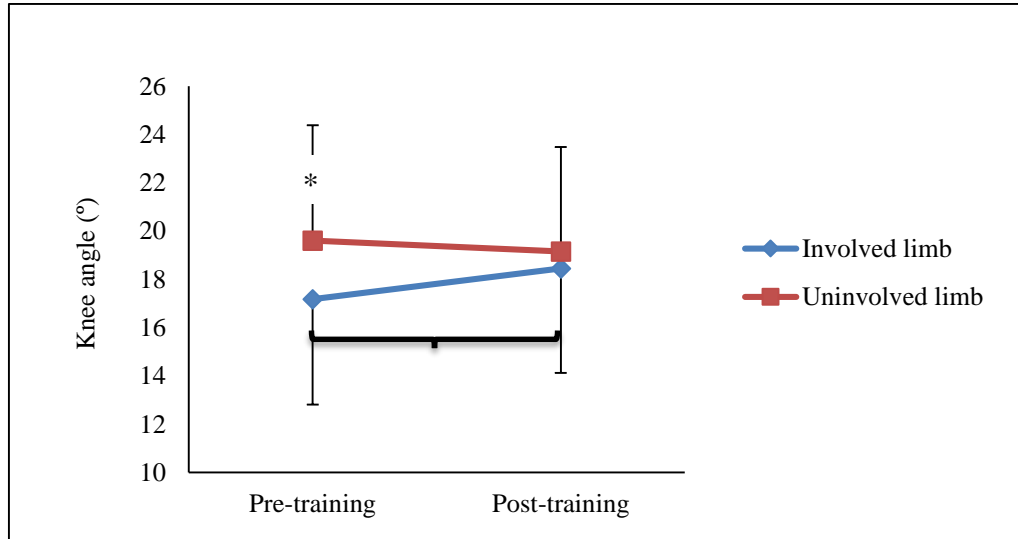


Figure 17 Knee excursion during WA between the involved and uninvolved limb at pre and post-training testing (Mean (SD); (*: Significant difference between limbs $P < 0.05$))

There was no significant group by time interaction for performance-based and patient-reported measures ($p \geq 0.20$). There was significant main effect of group for single hop LSI (manual: $79.68 \pm 15.27\%$, 3DOF: $99.44 \pm 13.21\%$; $p = 0.002$), cross-over hop LSI (manual: $81.24 \pm 15.287\%$; 3DOF: $95.58 \pm 13.35\%$; $p = 0.03$), triple hop LSI (manual: $75.43 \pm 11.71\%$; 3DOF: $95.76 \pm 8.28\%$; $p < 0.001$), and 6-meter timed hop LSI (manual: $81.59 \pm 7.69\%$; 3DOF: $96.86 \pm 6.66\%$; $p < 0.001$) with 3DOF group performed higher on the single-legged hop tests. Significant differences between the manual and 3DOF groups at pre-training testing were found for all of the single hop, cross-over hop, triple hop, and 6-meter timed hop LSIs ($p < 0.022$) with 3DOF group demonstrated higher scores (Table 12). At pre-training testing session, the 3DOF group demonstrated limb-to-limb symmetry as the means of the 3DOF group for QI, single-legged hop LSIs, and KOS-ADLS were $\geq 90\%$ (Table 12).

There was also significant main effect of time for single hop LSI with both groups decreased their single hop LSI (pre-training: $92.22 \pm 10.81\%$; post-training: $85.73 \pm 11.00\%$; $p=0.013$), triple hop LSI (pre-training: $81.73 \pm 9.42\%$; post-training: $89.43 \pm 6.96\%$; $p=0.023$), 6-meter timed hop LSI (pre-training: $82.78 \pm 8.85\%$, post-training: $95.66 \pm 9.09\%$; $p=0.007$) LSIs, and KOS-ADLS (pre-training: $86.91 \pm 9.95\%$; post-training: $90.73 \pm 6.53\%$; $p=0.043$) (Table 12) with subjects in both groups improving their symmetry on the single-legged hop tests and on the patient-reported measures at the post-training testing compared to the pre-training testing except for single hop LSI. Only one subject of the 3DOF group passed RTAC variables at pre-training testing session and 2 subjects (22%) of the 3DOF group passed the RTAC at the post-training testing session while no subject from the manual group passed the RTAC at either pre or post-training testing.

Table 12 Performance-based and patient-reported measures of manual and 3DOF groups at both pre and post-training testing (Mean (SD))

Variables	Pre-Training Testing		Post-Training Testing		Group*Time (p-value)
	Manual (n=9)	3DOF (n=9)	Manual (n=9)	3DOF (n=9)	
QI (%)	89.56 (11.95)	94.53 (15.15)	91.12 (12.97)	90.33 (13.42)	0.337
Single Hop LSI (%)	81.72 (9.55)	102.72 (11.47)	75.30 (14.23)	96.16 (7.67)	0.976
Cross-over hop LSI (%)	82.22 (13.17)	96.31 (9.66)	80.26 (19.82)	94.86 (9.76)	0.956
Triple hop LSI (%)	70.35 (6.07)	93.12 (9.86)	80.50 (7.50)	98.36 (6.14)	0.412
6-m timed hop LSI (%)	73.17 (11.77)	92.41 (5.71)	90.02 (13.13)	101.31 (4.02)	0.335
KOS-ADLS (%)	82.40 (13.95)	91.43 (5.87)	88.42 (7.92)	93.04 (6.22)	0.221
GRS (%)	77.22 (13.98)	73.11 (15.07)	77.80 (19.93)	78.78 (16.12)	0.2

4.8 Discussion

The purpose of this study was to investigate whether administration of perturbation training using mechanical device provides effects similar to manual perturbation training on knee kinematic and kinetic, performance-based, and patient-reported measures in patients with an acute ACL injury. The results of this study revealed that administration of perturbation training using mechanical device induced effects similar to manual perturbation training on knee mechanics, knee functional performance, and patient-reported knee function.

In this study we included both motion analysis and clinical testing to evaluate the effect of perturbation training that was administered using mechanical device and it was also compared to manual perturbation training. Gait motion analysis testing revealed that patients in both groups did not differ in the way they responded to the

two types of perturbation training. This finding was anticipated as the mechanical device provides perturbation stimuli similar to that of the manual perturbation training. In addition, the magnitudes of all perturbation stimuli parameters related to the amplitudes, velocities, accelerations, and directions were determined in our motion analysis laboratory during real-time manual perturbation training.

The gait motion analysis testing revealed that subjects in both groups improved their external knee flexion moment after perturbation training. This improvement may be resulted as subjects improved their knee functional performance and they may have started loading the involved knee more after perturbation training. The gait motion analysis testing showed a trend toward less limb-to-limb gait asymmetries after training. However patients continue to exhibit statically limb-to-limb gait asymmetries regardless of the treatment group. Prior training, patients in both groups demonstrated clinically important limb-to-limb asymmetries for knee motion during MS and external knee extension moment. Clinically important limb-to-limb asymmetries continued to exist after perturbation training for both groups; except the 3DOF demonstrated no clinically meaningful limb-to-limb asymmetry for knee excursion during MS interval. While these improvement were not statically significant, these improvement might have resulted from the underling differences between groups in stability classification as the 3DOF group included a mixed of subjects with dynamic knee stability (6 subjects) and subjects with dynamic knee instability while the manual group included only subjects with dynamic knee instability. Additionally, the 3DOF's improvement may be resulted from the agility training that five subjects of 3DOF group received. The 3DOF group also demonstrated limb-to-limb symmetry for each of quadriceps strength and functional

performance at pre-training testing compared to the manual group which may contributed to the improvement of that group. The improvements in the 3DOF group are similar to the results of a previous study by Chmielewski and colleagues ¹¹. Chmielewski's study investigated the effect of perturbation training on subjects with acute ACL injury who were classified as subjects with dynamic knee stability³⁶. The presence of statically limb-to-limb asymmetries in knee excursions after perturbation training was not anticipated and contradicts with what was reported in previous studies. In previous studies that investigated the effect of manual perturbation training on gait biomechanics of patients with ACL rupture reported that manual perturbation training helps mitigating abnormal knee motion^{11,15}. These studies, however, analyzed their data based on patients' sex and stability classification (included only patients with dynamic knee stability)^{8,11,15}. In this study, we did not stratify the data based on patients' sex or stability classification. With regard to the reduced involved limb external knee moments and limb-to-limb kinetic asymmetries were anticipated as previous studies reported similar finding after training and after ACLR^{14,15,30}. It has been reported that limb-to-limb gait asymmetries continue to persist long time after ACL rupture and even following reconstruction surgery^{14,30,67}. The limb-to-limb gait asymmetries alter the joint loading mechanism across different activities ^{107,143}. Previous studies reported patients after ACL rupture lean toward overloading the uninvolved limb which may result in overloading injuries to the uninvolved limb^{67,110}. In comparison, patient with limb-to-limb gait asymmetry lead to underloading the involved limb which may result in underloading injuries. The presence of limb-to-limb gait asymmetries is not favored in patients who have the desire to return to highly physical activities. Limb-to-limb gait asymmetries may

increase the risk for further knee injuries especially during participation in highly demand activities as these asymmetries get magnified^{43,144}. There is a growing evidence suggests that underloading the knee joint may associate with negative changes to the joint integrity^{42,145}. The presence of limb-to-limb asymmetries in this study may indicate that patients are required to participate in an extended rehabilitation program. In this study, each patient received 10-training sessions of perturbation training, future studies may consider evaluating the effect of an extended number of sessions of perturbation training on patients who continue to demonstrated limb-to-limb gait asymmetries. Restoring gait limb-to-limb gait symmetries is essential to preserve the joint integrity after ACL rupture and ACLR. furthermore, restoring normal limb-to-limb gait symmetries helps reduce abnormal joint loading mechanism and decrease the risk of a secondary injuries¹⁴⁶.

The clinical testing of this study also revealed that administering perturbation training using mechanical device provides effects similar to manual training on performance-based and patient-reported measures. The results of this study showed that patients in both groups improved their knee functional performance and patient-reported measures after perturbation training regardless of the perturbation type except for single hop and cross-over hops measures. Previous studies reported similar results that manual perturbation training enhances the knee function and patient-reported measures compared to other training programs^{5,14,30}. Both groups demonstrated reduction in their performance on single hop and cross-over hop LSIs measures. The 3DOF group also demonstrated a reduction in their performance on the QI measure after training. These reductions do not designate that the subjects in both groups reduced their involved limb's quadriceps strength and hoped for short distance on the

involved limb. Instead, these reductions in patients' performance on the previous mentioned measures resulted from improvements in the uninvolved limb quadriceps strength and hop performances. Improvements of the uninvolved limb can be explained as the perturbation programs included training for both the involved and uninvolved limbs.

The 3DOF group demonstrated significantly higher performance-based and scored higher on patient-reported measures compared to the manual group at pre-training testing session. Even though, subjects in both groups were recruited mainly from the University of Delaware's Physical Therapy Clinic and there was no significant difference between groups in the time from injury to the enrollment. The differences between groups at pre-training testing could be related to the patient's stability classification as 6 patients of 3DOF group had dynamic knee stability while all subjects in the manual group included only patient with dynamic knee instability. Patients with dynamic knee stability are those individuals who are able to resume preinjury activities level with no symptoms of dynamic knee instability for one year from the ACL injury^{8,12,147}. Patient with knee stability also walk with gait pattern similar to the healthy uninjured individuals^{35,52}. In comparison, patients with dynamic knee instability are patients who experience dynamic knee instability during simple daily activities^{7,8}.

While 3DOF group demonstrated symmetrical quadriceps strength and functional performance, limb-to-limb gait asymmetries continued to persist after training. This might indicate that limb-to-limb gait asymmetries cannot be resolved solely by attaining adequate quadriceps strength or functional performance. Resolving limb-to-limb gait symmetries may require an extended period of time for

neuromuscular recovery. Roewer and colleagues suggested restoring quadriceps strength does not resolve the limb-to-limb knee kinematics immediately after ACLR¹⁴. While the relationship between limb-to-limb functional symmetries and the gait limb-to-limb asymmetries has not established among patients with dynamic knee stability. Di Stasi and colleagues reported that patients with normal knee function and limb-to-limb functional symmetries demonstrated less limb-to-limb gait asymmetries⁹⁶. In this study we used groups' means of quadriceps strength and performance-based variables to describe whether 3DOF and manual groups demonstrated limb-to-limb symmetry but not each patient individually. Therefore, using groups' means may be misleading as they do not indicate that individual patient achieved limb-to-limb symmetry.

Most patients failed on RTAC after training, this might be due to one or multiple reasons including quadriceps strength deficit, lower performance of the involved limb on hop tests, and scoring lower on patient-reported measures. Patient may continue participation in progressive strengthening training and different neuromuscular training that include jumping, landing (i.e. plyometric training).

At the pre-training testing, the 3DOF group did not have limb-to-limb gait asymmetry in the external knee moments compared to the manual group even though clinically important limb-to-limb asymmetries existed. This higher external knee moment for the 3DOF group might be due to the fact that 6 out of the 9 patients were classified as patients with dynamic knee stability. Additionally, the 3DOF's group demonstrated normal quadriceps strength and normal limb-to-limb symmetry during functional tasks. Rudolph and colleagues reported that strong correlations between the quadriceps strength and the external knee flexion moment in patient with dynamic knee stability after ACL rupture¹⁴⁸. The 3DOF group achieved clinically meaningful

improvement in the external knee moment but was not significant. This might be also due to the fact that the 3DOF group had limb-to-limb symmetry for quadriceps and single-legged hop test and scored higher on the patient-reported knee functional measures at the post-training testing. Five patients of the 3DOF group pursued non-surgical management and received agility training in addition to the mechanical perturbation. While the study was underpowered to do such analysis, the statistical analysis revealed that there was no significant interaction or main effect of time for all the biomechanical variables ($P > 0.05$). Significant main effect of groups (those who received agility vs who did not receive agility) was found for the knee excursion during WA and for the external knee flexion moment ($p < 0.05$) with those subjects who did not receive agility training had larger knee excursion and moment.

The manual perturbation training included more training technique (rockerboard) which requires longer training time from the treating therapist compared to the 3DOF training protocol. However, the results of this study shown that there were no differences between the perturbation training that was administered mechanically using automated device or manually by a physical therapist. The rockerboard might provide less contribution to the benefit of the perturbation training on the knee mechanics and functional performance. There are contradicting results in literature about the effect of the rockerboard as prevention and rehabilitation training for ankle sprain^{149–152}. The rockerboard training targets mainly the ankle joint and the muscles of the leg and foot, and it may has indirect effect on the knee joint or the muscles that cross the knee joint. Additionally, the directions of the rockerboard training of the manual training are oriented toward the medial-lateral and diagonal directions (less to anterior-posterior). In this study the mechanical perturbation stimuli

were identical to that of the manual training; therefore the results of this study suggest that the rockerboard may not be effective training after ACL rupture. Further research may consider evaluating the effect of rockerboard on the neuromuscular responses, knee biomechanics, and knee functional performance in patients with ACL rupture.

4.9 Limitation

One limitation of this study was the usage of a data from a previous study (manual group) to serve as a comparison group. There was groups' difference in the patients' stability classification between the manual and 3DOF groups (3DOF group had subjects with dynamic knee stability compared to manual group). Other studies accounted for patients' sex and stability classification in their data analysis^{11,15}, while we did not include patients' sex and stability classification in the analysis of this study due to small sample size. There was a limitation that may be associated with training on the mechanical device as the therapist cannot physically sense whether the patient responses appropriately through selective muscle activation compared to manual perturbation training. In addition, the usage of LSIs to evaluate the subjects' responses to therapeutic interventions or involved knee function improvement in comparison to the uninvolved limb. LSIs may lead to misinterpretation of the results as it is possible that both the involved and uninvolved limbs improve their performance after intervention^{153,154}. In this study the LSIs of single hop and cross-over- hop were lower at post-training testing compared to the pre-training testing in the 3DOF group. However, subjects hopped for farther distance on the involved and uninvolved limbs on the single hop and cross-over hop tests at post-training testing session. Therefore, reporting the absolute values for the involved and uninvolved limbs provides more information about changes in the involved limb functional performance.

4.10 Conclusion

The clinical and motion analysis testing of this study show that administering perturbation training using mechanical device provides effects similar to manual perturbation training on knee mechanics, knee functional performance, and patient-reported measures of patients with an acute ACL rupture. The result of this study revealed that patients demonstrated gait limb-to-limb asymmetry after the training regardless of the treatment group. The presence of limb-to-limb gait asymmetries may indicate that patients require participation in an extended rehabilitation program to restore normal knee motion and function and to resolve limb-to-limb gait asymmetries.

Chapter 5

EFFECT OF MANUAL AND PERTURBATION TRAINING ON PATIENTS AFTER ANTERIOR CRUCIATE LIGAMENT RUPTURE

5.1 Abstract

Background: Majority of patients with ACL rupture demonstrate maladaptive neuromuscular changes to stabilize the knee joint. These changes compromise the knee motion and increase the compressive forces between the articular surfaces of the knee. Manual perturbation training is an effective intervention that improves the dynamic knee stability and reduces muscle co-contraction, and promote selective muscle activation pattern. It is unknown whether providing perturbation training using mechanical device induce effects similar to manual perturbation training on the neuromuscular strategies of patients with ACL rupture.

Purpose: To investigate whether administration of mechanical perturbation training provides similar effects as manual perturbation training on time duration of onset-to-peak muscle activity and muscle co-contraction indexes, and whether changes in the onset-to-peak muscle activity associate with the muscle co-contraction indexes.

Materials: Eighteen level I or II subjects with acute ACL rupture participated in this study. Nine subjects received mechanical perturbation training (3DOF group) and 9 patients matched by sex and age received manual perturbation training (manual group). All subjects completed a pre and post-training testing that include 3-D gait motion analysis and surface electromyography of the quadriceps (VM and VL), hamstring (MH and LH), gastrocnemius (MG and LG), and soleus (SOL) muscles. Muscle co-contraction index was calculated for the medial and lateral sides of both quadriceps-hamstring and quadriceps-gastrocnemius muscle pair during stance phase of gait. Muscle timing variable (Onset time-to-peak muscle activity in millisecond

(ms)) was calculated for quadriceps, hamstring, gastrocnemius, and soleus muscle groups.

Results: No significant group by time by limb interaction was found for the onset time-to-peak muscle activity and muscle co-contraction indexes ($p \geq 0.30$). Significant group by time interaction was found for onset-to-peak muscle activity of VM ($p=0.095$) with significant differences between groups were found at pre and post-training testing sessions ($p < 0.001$).

Significant group by time by limb interaction was found for LH-VL during TS ($p=0.059$) with the involved limb had significantly higher co-contraction and the uninvolved limb of 3DOF group increased LH-VL muscle co-contraction during TS significantly after training. Significant group by time interaction was detected for LG-VL muscle co-contraction during WA ($p=0.064$) with 3DOF group having significantly higher co-contraction after training and the manual group decreased LG-VL muscle co-contraction during WA after training. Significant group by limb was found for the LG-VL muscle co-contraction during MS ($p=0.097$) with 3DOF group demonstrated significant lower LG-VL muscle co-contraction during MS of the uninvolved limb ($p=0.006$).

Moderate to strong relationship between time duration of onset-to-peak muscle activity and the magnitude of muscle co-contraction indexes at both pre and post-training testing sessions throughout the stance phase of the gait cycle ($p < 0.1$). The change in onset time-to-peak muscle activity of muscles between pre to post-training had moderate to strong correlation with the muscle co-contraction indexes at post-training testing ($p < 0.1$).

Discussion: Administering perturbation training using mechanical device provides effects similar to manual perturbation training on neuromuscular compensation including muscle activation timing and muscle co-contraction. Perturbation training attempts to resolve neuromuscular deficits and restore a balance in muscle activation between knee flexors and extensors to provide dynamic joint stability. The magnitude of muscle co-contraction index is influenced by the length of time duration of muscles' activities. The relationships between time duration of muscles' activities and muscle co-contraction may indicate that perturbation training induce a neuromuscular adaptation to provide dynamic knee stability.

5.2 Introduction

The anterior cruciate ligament (ACL) is the primary stabilizer of the knee joint, limiting motion in the anterior-posterior and rotational demands^{53,155}. Rupture of the ACL is a common sport related injury of the knee joint. The hallmark symptom of the ACL rupture is knee instability which has negative short and long term consequences on knee joint structures and on functional performance of the involved limb⁹. While some patients adapt successful dynamic knee stabilization strategies during different level of physical activities, most of patients experience dynamic knee instability even with simple daily activities⁸. Those patients who experience dynamic knee instability adopt abnormal neuromuscular strategy characterized by knee stiffening and gross muscle co-contraction of knee flexor and extensor muscles to compensate for the loss of passive knee restraint^{6,11,51}. Increased muscle co-contraction is considered as a protective mechanism that stabilizes the knee joint as it reduces shear forces between the joint surfaces, and reduces translation at the knee joint¹⁵⁶. Increased muscle co-contraction, however, compromises normal knee movements during functional

activities (i.e. reduced knee motion and external knee moments) and increases the net compressive forces between the articular surfaces^{6,11,51,47,157}.

During functional activities, knee flexor muscles alter their activation pattern (magnitude of muscle activity and duration time) to oppose the potential knee joint instability^{35,148,158}. Knee flexor muscles work as an agonist for the ACL that provide stability to the knee joint¹⁵⁸. During gait, the quadriceps muscle contractions (eccentric or concentric) cause an anterior translation of the proximal tibia¹⁵⁸. In response to that, a simultaneous co-contraction of the hamstring and gastrocnemius muscles occur to stabilize the knee joint resulting in what so called muscle co-contraction¹⁵⁸. The long-lasting of maladaptive neuromuscular pattern, muscle co-contraction and knee stiffness, may have negative impacts on patient's performance during highly demand activities^{43,144}. Furthermore, it may have a negative impact on knee joint integrity as it might increase the contact force of the joint's articular surfaces and cause an initiation or progression of knee osteoarthritis^{43,49}.

Numerous studies investigating the muscle activity using electromyography data reported that patients with ACL rupture demonstrate an increased magnitude of knee flexor muscles activities during the stance phase of gait cycle and increased knee extensor-flexor muscles co-contraction of the involved limb^{6,147,159}. These changes correspond with increase in the magnitude of knee flexor muscles activity, prolonged knee flexor muscles activities, delayed peak muscle activity, and longer total duration time of the onset-to-peak muscle activity of the involved limb^{12,160,161}.

The abnormalities in the gait pattern (i.e. reduced external knee moments and reduced knee motion) are consistent among majority of patients with ACL rupture^{12,35,45,157,158}. Studies with electromyography data revealed that these gait

abnormalities are related to the changes in the knee flexor muscles activation^{12,157,162}. The knee flexor muscles respond by altering the pattern of muscle activation pattern (i.e. magnitude and the time duration of muscle activity) as a protection mechanism attempt to stabilize the knee joint^{6,163}. Majority of patients with ACL rupture demonstrated delayed peak muscle activity and longer duration between onset-to-peak muscle activities for knee flexor muscle^{12,48}. These delay indicate that the knee flexor muscle are not generating enough force at an appropriate time to control the external moments applied on the knee joint during walking. This in turn may cause the knee joint to give way during dynamic functional activities. Beard and colleagues reported a relationship between delayed knee hamstring muscle activities in patients with ACL rupture and episodes of knee giving ways⁴⁸. The association between the magnitude of knee flexor muscles activation and the duration of onset-to-peak muscle activation, however, has not been defined.

Resolving knee impairments related to joint effusion, range of motion, quadriceps strength, and neuromuscular dysfunction is crucial for patient functional performance after ACL injury. Additionally, identifying and implementing appropriate interventions to resolve maladaptive neuromuscular patterns and restore normal movement pattern that may preserve the joint health and enhance patient's performance during participating in high demand activities. Perturbation training, a specific neuromuscular training, is the recommended therapy for patients with ACL rupture⁵³. Manual perturbation training has been shown to be an effective intervention that improves dynamic knee stability and function, normalizes the knee motion, reduces muscle co-contraction, and promote selective muscle activation pattern^{5,11,15,164}. Manual perturbation training is not commonly used among

rehabilitation settings. Additionally, manual perturbation training requires an extensive physical labor and one-on-one time from the treating therapist. Administering perturbation training using mechanical device facilitates the use of the training in a wide range of rehabilitation settings. Additionally, it also allows administration of controlled and standardized perturbation stimuli with an attempt to optimize the ACL rehabilitation programs.

The mechanical perturbation devices have been widely used for testing purposes and to provide therapeutic training for patients with different neurological and musculoskeletal impairments^{55,58-60,139-141}. Administration of mechanical perturbation training enhances the proprioceptive system re-educating, improves mechanoreceptor function, and alleviates abnormal neuromuscular coordination⁵⁵⁻⁵⁷. Mechanical perturbation also has the potential to improve the balance abilities⁵⁵, increase postural reflex by reducing reaction time⁵⁸, improve balance and stability in patients with OA⁵⁹, and enhance the timing and pattern of muscle activation⁶⁰. The effect of mechanical perturbation training on the neuromuscular strategies (magnitude of muscle activity and timing parameters) of patients with an ACL deficiency is yet unknown.

Additionally, little is known about whether the perturbation training can alter the time duration of the muscle activation and whether there will be an association between altering the time duration of muscle activation and the magnitude of muscle co-contraction during gait. Beard and colleagues reported that the duration of hamstring muscle activity during early stance correlated strongly with the knee flexion angle at foot contact and moderately with the knee flexion angle during mid-stance interval¹⁶³. Hurd and colleagues reported that manual perturbation training induced a

change in time duration of muscle activity in healthy female individuals⁵¹. Hurd's study report that administering manual perturbation training induced a shift in the onset-to-peak muscle activity for medial hamstring as it was moved from after to before heel strike. To this end, it is unknown whether perturbation training will restore the normal time duration of muscle activity in patients with acute ACL rupture. Therefore the purpose of this study was to investigate whether administration of 10-training sessions of mechanical perturbation training using the 3DOF plate provides effects similar to 10-sessions of manual perturbation training on neuromuscular compensation including muscle activation timing and muscle co-contraction indexes measures in the involved limb and to determine how these compensations change over the progression of perturbation training. Additionally, the purpose of this study was to investigate whether there will be a relationship between the time duration of onset time-to-peak muscle activity and the muscle co-contraction indexes, and whether changes in the time duration of onset time-to-peak muscle activity from pre to post-training testing associate with the muscle co-contraction indexes.

5.3 Methods

Eleven subjects (women: 4, men: 7) with an acute isolated unilateral ACL rupture (< 7 months) were enrolled into this pilot study. Subjects between the ages 14-55 (mean: 21.32 ± 5.52 year) were regular participants in level I or II sport activities that include jumping, cutting, pivoting, and lateral movements (i.e. soccer, football, rugby, tennis, ice hockey, and wrestling) for at least 50 hours per year prior to their ACL injury⁷. Subjects with previous serious lower extremities injury (i.e. fracture), concurrent multiple ligamentous injury, repairable meniscus, osteochondral defect (>1 cm²), or demonstrated less than a 3 mm side to side difference in passive anterior knee

laxity measured with a KT-2000 arthrometer⁸⁹ were excluded from the study. The ACL injury and concomitant knee injury were determined using both physical examination and magnetic resonance imaging (MRI). Subjects in this study were primarily recruited through the University of Delaware Physical Therapy Clinic. The study was approved by the University of Delaware Institutional Human Subjects Review Board. All subjects provided written informed consent for participation in this study.

Subjects were assigned to receive 10-training sessions of perturbation treatment using a mechanical device “Reactive Agility System” (3DOF group). The Reactive Agility System device was developed by Simbex LLC (Lebanon, NH). The mechanical device a movable plate that provides mechanical perturbation training by moving into different direction along the X and Y direction with optional rotations (10°) around the Z axis (3DOF group). The 3DOF plate provides mechanical stimuli that are executed randomly in combinations of three amplitudes (small, medium, and large), three velocities (low, medium, and high), and in eight directions and two optional rotation directions.

The maximum velocity and acceleration limits of the 3DOF plate during the planar translations were 400mm/ sec and 25000 mm/sec² and during the rotational translation were 120°/sec and 10000°/sec² respectively. The 3DOF plate provided three perturbation amplitudes: short: 22mm; medium: 33mm; long: 45mm and three planar velocities; low: 75mm/sec; medium: 150mm/sec; high: 250mm/sec. The parameters of the 3DOF mechanical perturbation (direction, amplitude, velocity, and acceleration, and deceleration) were measured using motion analysis system in our motion analysis laboratory during real-time manual perturbation training previously

described by Fitzgerald⁵. The manual perturbation, however, included the rockerboard technique which was not part of the 3DOF mechanical perturbation training program. The complete 3DOF perturbation training protocol is outlined in Appendix A. Two subjects (women: 2, men: 0) were enrolled into the study and dropped out. One subject developed neurological symptoms (numbness, tingling) in one side of the body before she started the training sessions, therefore she was withdrawn from the study as the neurological symptoms may interfere with the training program of this study. The other subject had a give-way episode at home, unrelated to her participation in the study, after the 6th training sessions. This patient demonstrated a massive knee effusion and her reconstruction surgery was scheduled too soon to resolve the knee impairments and complete the rest of training sessions (Figure 18).

In addition to the 9 subjects in 3DOF group, 9 subjects from a previous study entitled “Can Neuromuscular Training Alter Movement Patterns? Study”^{15,142} matched by age and sex were used to serve as a comparison group (Manual group) (Figure 18). The manual perturbation training program included administration of 10-training sessions of purposeful manipulation of the support surfaces including rockerboard, rollerboard, and rollerboard and platform by a physical therapist similar to that previously described by Fitzgerald et al⁵.

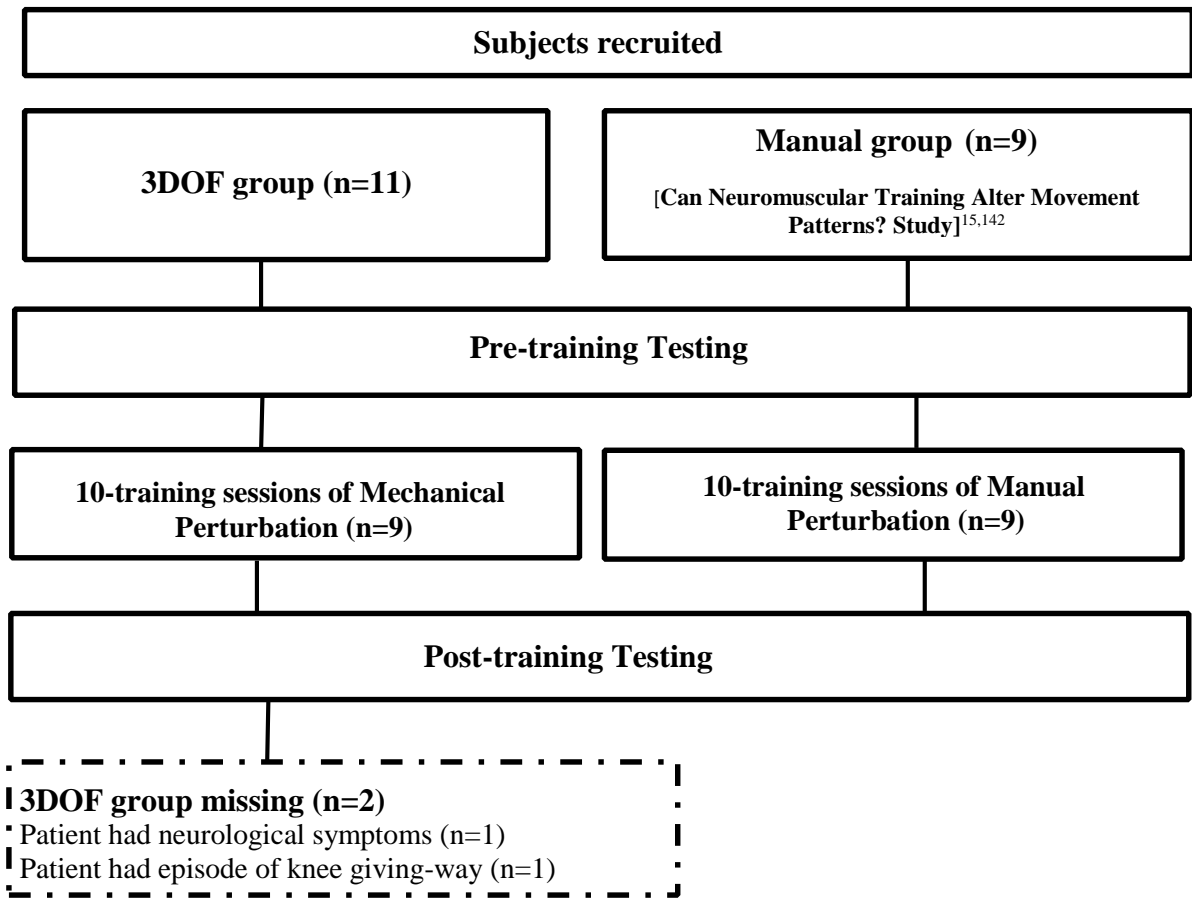


Figure 18 Patient enrollment and participating in the study

Five subjects from 3DOF group who choose to pursue a long term non-surgical management and received agility drill training. All subjects in the manual group were scheduled for reconstruction surgery; therefore all of the subjects in the manual group did not receive agility training. Agility drill training was administered at the end of each training session with all subjects wearing knee functional brace to improve subjects' lower extremities muscles neuromuscular coordination and to increase patients' ability to quickly change running directions⁹⁷. Agility training was initiated for subjects if they reported no episode of knee instability "giving way" since their

ACL injury and achieved full knee range of motion (ROM), minimum effusion, and pain-free with loading activities. Agility techniques included forward and backward running with quick start and stop, side shuffling, carioca, figure-eight running, and 45-degree cutting and sprinting, and 90 degrees cutting maneuvers. Subjects began performing agility training at 35% to 50% of their maximum effort and progress to full-effort training over the 10-training sessions. Perturbation training (3DOF or Manual) and agility training were progressed based on the subject's tolerance for training and if the subjects reported no joint pain, soreness, or development of knee effusion. Sport-specific tasks (basketball dribbling, ball throwing, ball kicking) were also integrated into the perturbation training (Manual and 3DOF) during the end phase of perturbation training (last three training sessions) when the subjects demonstrated minimal balance disturbance and minimal co-contraction responses during perturbation training. Subjects who received agility training were progressed once they demonstrated tolerance for full-effort training without pain or swelling⁹⁷. In addition, subjects in both groups with $QI < 80\%$ received a supervised progressive strengthening training augmented with neuromuscular electrical stimulation (NMES) to improve the quadriceps strength, while subjects with $80 \leq QI \leq 90\%$ received supervised progressive strengthening training with no NMES training. Subjects with $QI \geq 90\%$ were instructed to start a fitness strengthening program to improve their quadriceps strength²⁴.

5.4 Testing

Surface electromyography (EMG) data was collected during each of the pre and post-training gait motion analysis testing using MA-300 EMG System (Motion Lab Systems, Baton Rouge, LA). Isopropyl alcohol and non-sterile gauze pads were used to abrade and clean the skin prior to the application of pre-amplified, stainless

steel, bipolar surface electrodes with a double differential configuration (38x19x8mm preamp size, 2 X 12mm disk diameter with a 18mm inter-electrode spacing, and a 12x3 mm bar between the disks; input impedance >100m Ω , CMRR > 100 dB at 65Hz). Electrodes were placed mid-muscle belly and parallel to the muscle fibers on the vastus lateralis, and vastus medialis (VL, VM), lateral and medial hamstrings (LH, MH), lateral and medial gastrocnemius (LG, MG), and soleus (SOL) muscles. Data was collected at a sampling rate of 1080 Hz. For each muscle, a 4-second maximum voluntary isometric contractions (MVIC) was completed and used for normalization in post processing. Each muscle's MVIC was visually inspected to verify signal quality, with gains adjusted when necessary to avoid signal clipping. A 2-second resting trial was collected for all muscles and used to define a window where no muscle activity was present. The mean of the resting window was subsequently used determining threshold for onset/offset of activity (3 times the resting mean). EMG data were initially band pass filtered in the hardware from 20-2000 Hz, with an anti-aliasing filter of 1000Hz and output voltage of ± 5 volts. Data were analog-to-digital converted via a 16-bit A to D board. Time-normalized EMG data was synced with motion data.

Data was post processed using Visual 3D (C-Motion Inc., Germantown, Maryland). The mean of the raw EMG data was computed and then subtracted from raw EMG data for each muscle to control for DC offset. Data were then band pass filter (30-350 Hz) and a linear envelope was created by full-wave rectification and low pass filter (6 Hz) using second-order, phase-corrected, Butterworth filters. The linear envelope for each muscle was then normalized to the muscle's maximum activity, identified either during MVIC testing or the walking trials. MVIC for gastrocnemius was tested during standing with the patient holding a countertop for providing

resistance while plantar flexing their feet. Quadriceps muscle was tested in a seated position with knee at 60° flexion and ankles were secured into a table through padded cuffs. Tibialis anterior muscle was tested in a long sitting position with patients' knees in an extended position and ankles were secured into a table. Hamstring muscle was tested while subject lying in prone position with the ankles secured into a table and knees were 30° flexion position. Finally SOL muscles were tested in quadruped positions with knees flexed to 90 degree and both feet were secured into a table in full dorsiflexion position.

Muscle co-contraction indexes, defined as the simultaneous activation of the agonist and anti-agonistic muscles (VL-LH, VM-MH, VL-LG, and VM-MG), were calculated from the corresponding muscles' linear envelope using the following formula:

$$co - contraction\ index = \left(\frac{\text{less active muscle}}{\text{more active muscle}} \right) \times (\text{less active muscle} + \text{more active muscle})^{12}.$$

Muscle co-contraction index for each muscle pair was averaged during the three intervals of the gait stance phase: weight acceptance (WA), mid-stance (MS), and terminal stance (TS) interval. The WA interval was defined from 100ms prior to heel strike (to account for electromechanical delay¹⁶⁵) to the point of peak knee flexion (PKF). The MS interval was defined from PKF to peak knee extension (PKE) and the TS interval from PKE to toe-off.

Muscle timing variables (Onset time-to-peak muscle activity in millisecond (ms)) for LG, MG, MH, LH, VM, VL, and SOL muscles were computed using the linear envelope of the corresponding muscles during walking trials. Muscle onset event for each muscle was calculated during gait stance phase, defined from 100ms prior to heel strike to toe-off, using a threshold of 3 times the mean of the resting trial.

Peak muscle activity for each muscle was computed as the maximum EMG activity during the gait stance phase. Onset time-to-peak muscle activity time difference between the pre and post-training testing was calculated as by subtracting the onset time-to-peak muscle activity at pre-training from the onset time-to-peak muscle activity at post-training (onset-to-peak muscle activity at pre-training - onset-to-peak muscle activity at post-training).

5.5 Statistics

Independent t-test was used to compare mean differences between 3DOF and manual groups for subjects' demographics, muscle co-contraction index, and onset time-to-peak muscle activity variables at pre-training testing session. Paired t-test was also used to determine significant differences between limbs for muscle co-contraction and onset time-to-peak muscle activity variables between at pre-training testing session. A 2x2x2 analysis of variance (ANOVA) was used to evaluate differences between treatment groups (between-subjects factor: manual and 3DOF), over time (within-subjects factor: pre-training and post-training), and between limbs (involved limb vs uninvolved limb) for muscle co-contraction and onset time-to-peak muscle activity variables. In case of significant interaction both independent and paired t-tests were used as post hoc testing. Independent t-tests were used to determine whether the significant difference for muscle co-contraction and onset time-to-peak muscle activity variables exists between group at either pre or post-training testing session. Paired t-tests were also used to determine whether 3DOF or manual groups demonstrated significant changes for muscle co-contraction and onset time-to-peak muscle activity variables between the pre and post-training testing sessions. Paired t-tests were also used to determine whether significance difference exists between limbs. Bivariate

correlation test was used to determine whether there was a relationship between onset time-to-peak muscle activity and muscle co-contraction at pre and post-training testing sessions. Bivariate correlation test was used to determine whether there was a relationship between the difference onset time-to-peak muscle activity from pre-to-post-training testing session and muscle co-contraction index. Significance level for muscle co-contraction and onset-to-peak muscle activity variables was established at $p < 0.1$ to account for the highly variability in the EMG data in order to avoid a type I error¹⁶⁶. Significant level for subjects' demographics was established at $P < 0.05$. All statistical analyses were performed using the SPSS 22.0 (IBM Company, Chicago, Illinois, USA).

5.6 Results

Nine subjects form the 3DOF group and 9 subjects matched by age and sex from a previous study (manual group) completed the pre and post-training testing and 10-training sessions of perturbation training. At pre-training testing session, there was no difference in percentage of women to men, age, and time from injury to the pre-training testing session between the 3DOF and manual groups ($p \geq 0.233$). The BMI, however, was significantly different between the groups with the manual group demonstrated larger BMI compared to the 3DOF group ($p = 0.044$) (Table 13).

Table 13 Patient's demographic for Manual and 3DOF groups at pre-training testing (Mean(SD))

Variables	3DOF group (n=9)	Manual group (n=9)	P-value
Subjects #(women/men)	9 (2/7)	9 (2/7)	0.712
Age (year)	21.32 (5.52)	22.23 (5.54)	0.731
BMI (N/M²)	24.13 (3.67)	28.17 (4.15)	0.044
Time from injury to pre-testing session (month)	1.93 (1.39)	1.13 (1.37)	0.233
Walking velocity	1.56 (0.14)	1.53 (0.13)	0.576

5.6.1 Onset-to-peak muscle activity

Walking velocity during motion analysis testing was not different between the 3DOF and manual groups ($p=0.576$). There was no significant group by time by limb interaction for the onset time-to-peak muscle activity for all muscles ($p=0.30$) (Figure 19). There was significant group by limb interaction for VM onset-to-peak muscle activity ($p=0.095$). Post hoc test revealed that there were significant differences between groups for onset-to-peak muscle activity of VM at pre and post-training testing sessions ($p<0.001$) (Figure 20). Significant time by limb interactions was found for onset-to-peak muscle activity of MG ($p=0.049$) and SOL muscles (0.033). Post hoc test revealed that there was significant difference between limbs for onset-to-peak muscle activity of MG at post-training testing session ($p=0.016$) with the involved limb demonstrating short time duration (Figure 21). Post hoc test also revealed that subjects decreased significantly the involved limb onset-to-peak muscle activity of SOL muscle ($p=0.086$) (Figure 22).

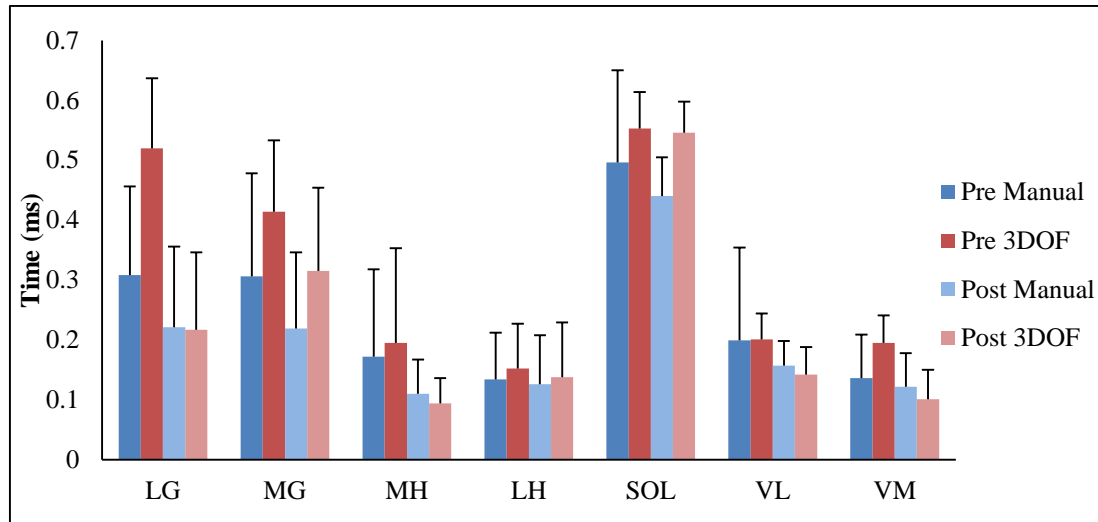


Figure 19 Onset-to-peak muscle activity of manual and 3DOF groups at pre and post-training testing (Mean (SE))

Significant main effect of group for onset-to-peak muscle activity was found for LG muscle (3DOF: 0.520 ± 0.107 ms; manual: 0.276 ± 0.107 ms; $p < 0.001$) and MG muscle (3DOF: 0.425 ± 0.099 ms; manual: 0.276 ± 0.093 ms; $p = 0.005$) with the 3DOF group demonstrated significant longer period of onset time-to-peak muscle activity compared to the manual. At pre-training testing, there were significant differences between manual and 3DOF groups in onset time-to-peak muscle activity at pre-training testing for all of LG ($p < 0.001$), MG ($p = 0.089$), and VM ($p = 0.057$) of the involved limb with the 3DOF group demonstrated longer onset time-to-peak muscle activity. A significant main effect of limb was found in the MH (involved: 0.161 ± 0.082 ; uninvolved: 0.110 ± 0.028 ; $p = 0.066$), with the MH muscle of the involved limb demonstrated longer onset time-to-peak muscle activity.

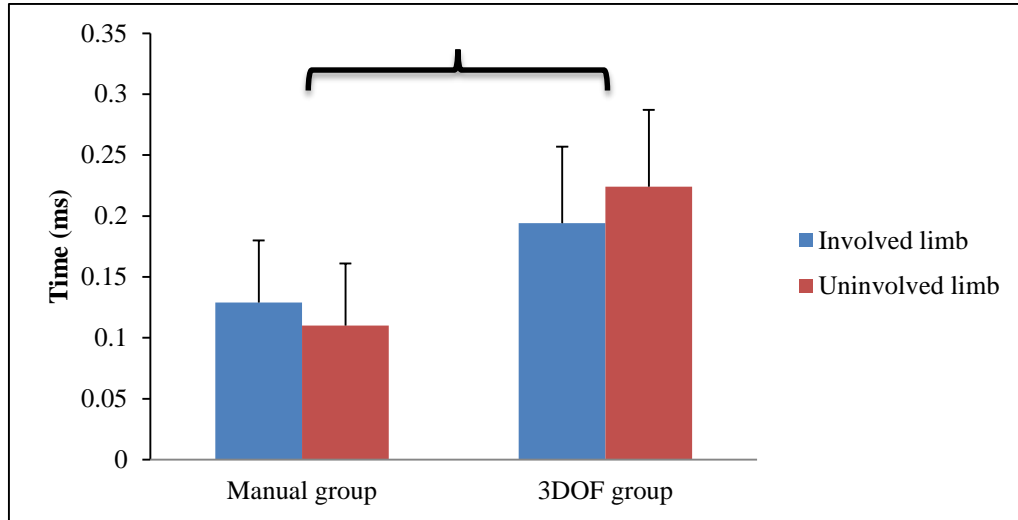


Figure 20 Onset-to-peak muscle activity of VM of manual and 3DOF groups at pre and post-training testing (Mean (SD))

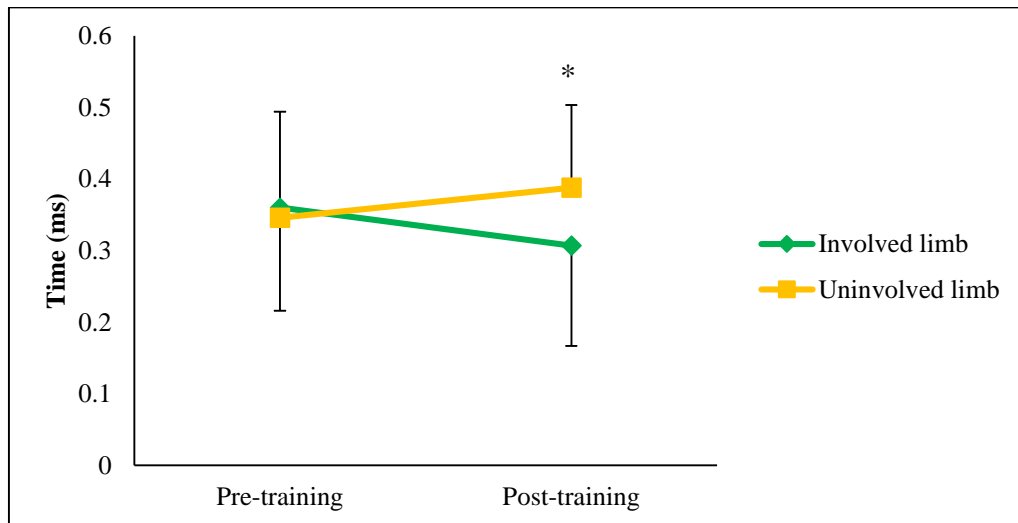


Figure 21 Onset-to-peak muscle activity for MG of the involved and uninvolved limbs at pre and post-training (Mean (SD); (*: Significant difference between limbs $P < 0.1$))

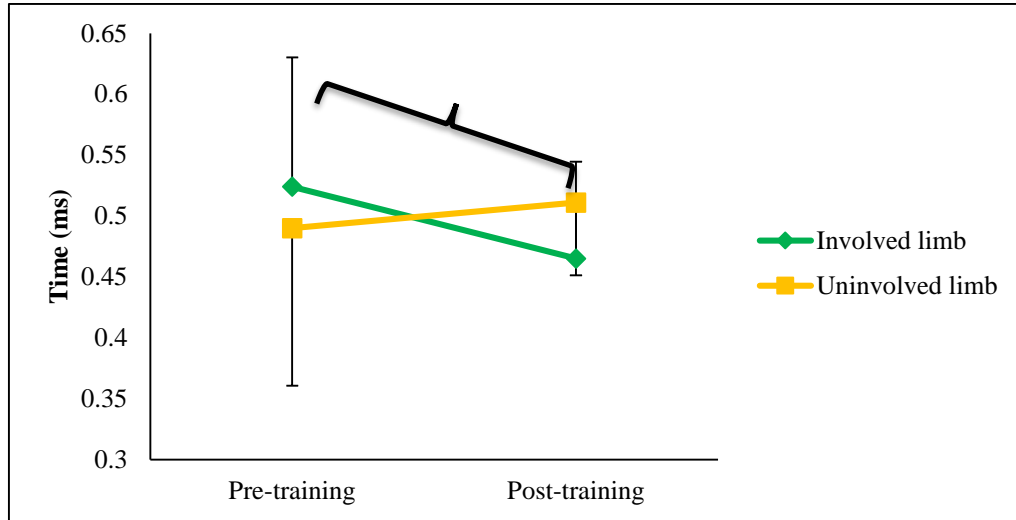


Figure 22 Onset-to-peak muscle activity for SOL of the involved and uninvolved limbs at pre and post-training (Mean (SD))

5.6.2 Muscle co-contraction

There was a significant group by time by limb interaction found for LV-LH muscle co-contraction index during TS ($p=0.059$) (Figure 23, 24, and 25). Post hoc test revealed that there was significant differences between limbs of 3DOF group at pre-training testing session ($p=0.002$) with the involved limb demonstrated higher LH-VL muscle co-contraction during TS. Post hoc test also revealed that uninvolved limb of 3DOF group increase LH-VL muscle co-contraction significantly during TS after training (Figure 25, 26 and 27).

Significant group by time interaction was detected for LG-VL during WA ($p=0.064$). Post hoc test revealed that significant difference between groups was found for LG-VL muscle co-contraction index during WA at post-training testing ($p=0.005$) with the 3DOF group demonstrated higher muscle co-contraction index (Figure 28). Post hoc test also revealed that manual group decreased significantly LG-VL muscle co-

contraction during WA after training ($p=0.05$) and 3DOF group increased significantly LG-VL muscle co-contraction during WA after training ($p=0.05$) (figure 28).

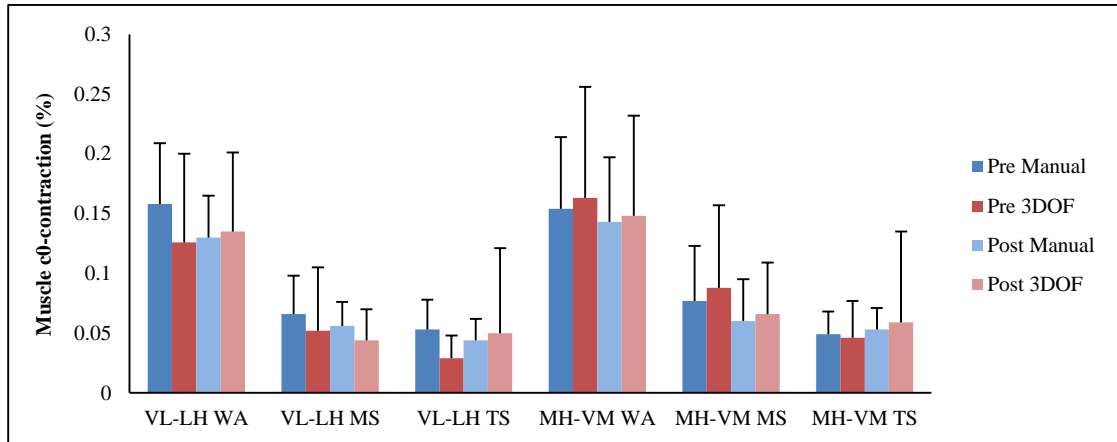


Figure 23 Quadriceps-Hamstring muscle co-contraction indexes of manual and 3DOF groups at pre and post-training testing (Mean (SE))

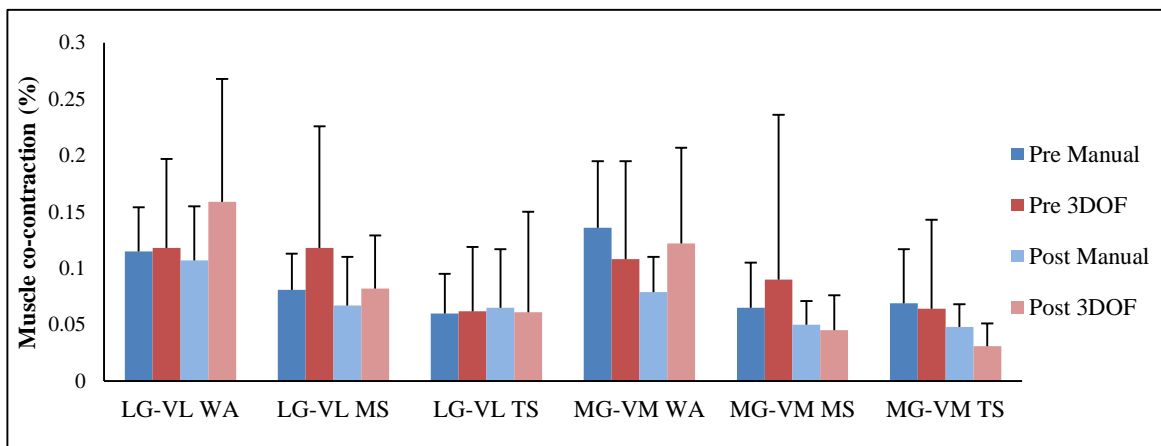


Figure 24 Quadriceps-Gastrocnemius muscle co-contraction indexes of manual and 3DOF groups at pre and post-training testing (Mean (SE))

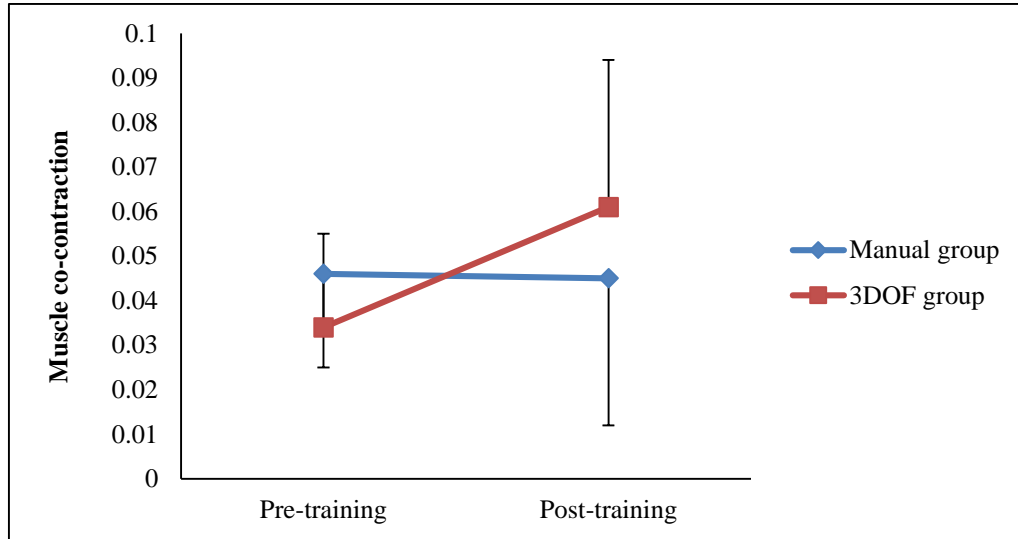


Figure 25 LH-VL muscle co-contraction during TS of manual and 3DOF groups at pre and post-training testing (Mean (SD))

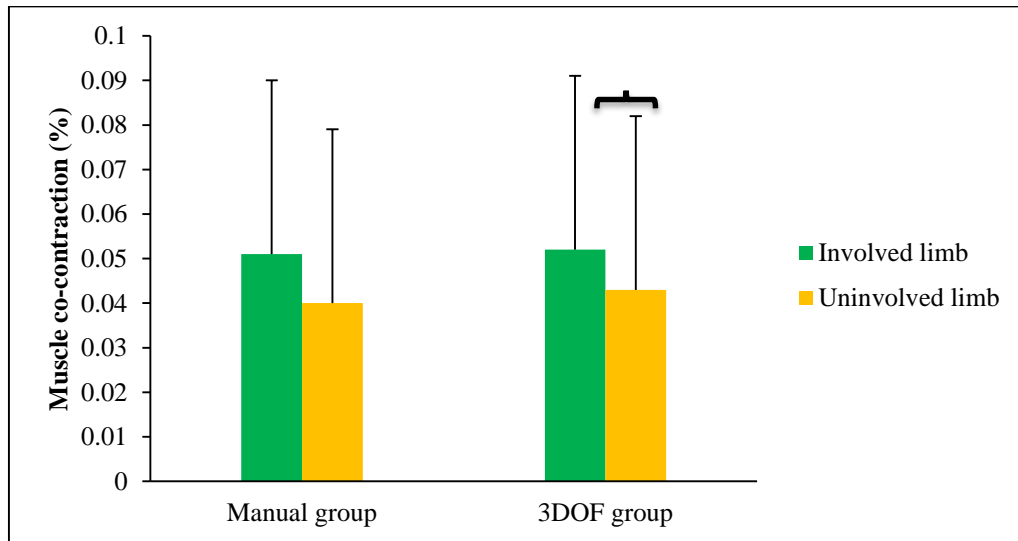


Figure 26 LH-VL muscle co-contraction index during TS for the involved and uninvolved limb of manual and 3DOF groups (Mean (SD))

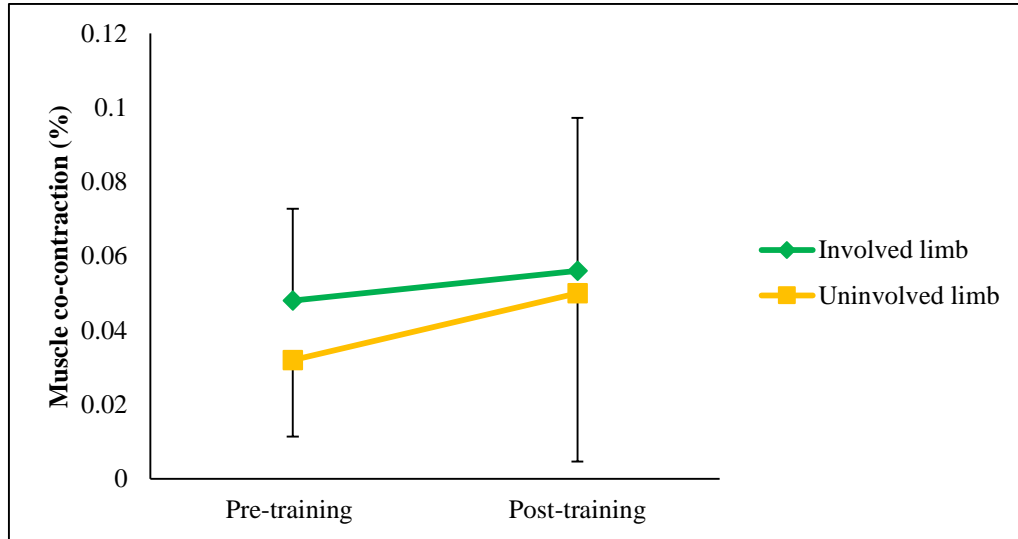


Figure 27 LH-VL muscle co-contraction during TS for the involved and uninvolved limb at pre and post-training (Mean (SD))

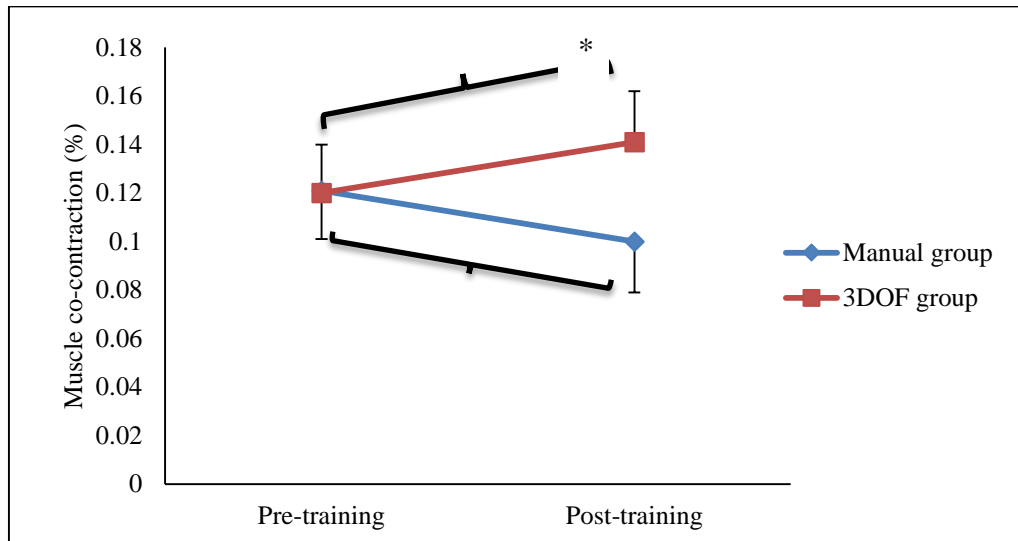


Figure 28 LG-VL during WA of manual and 3DOF groups at pre and post-training testing (Mean (SD); (*: Significant difference between groups $P < 0.1$))

Significant limbs by time interaction was found for the LG-VL muscle co-contraction during WA ($p=0.04$). Post hoc revealed that there was significant difference between limbs at post-training testing session ($p=0.049$) with the involved limb had higher muscle co-contraction index (Figure 29). Significant group by limb was found for the LG-VL muscle co-contraction during MS ($p=0.097$). Post hoc test revealed that there was significant differences between the involved and uninvolved limbs in LG-VL muscle co-contraction during MS ($p=0.016$). Post hoc also revealed that 3DOF group demonstrated significant lower LG-VL muscle co-contraction during MS of the uninvolved limb ($p=0.006$) (Figure 30).

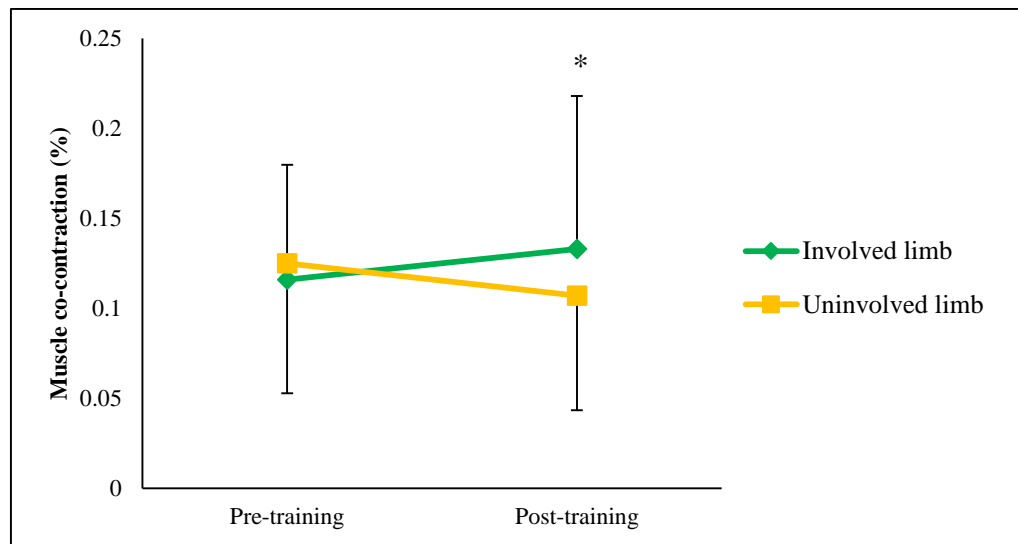


Figure 29 LG-VL muscle co-contraction during WA for the involved and uninvolved limbs of manual and 3DOF groups at pre and post-training testing (Mean (SD); (*: Significant difference between groups $P < 0.1$))

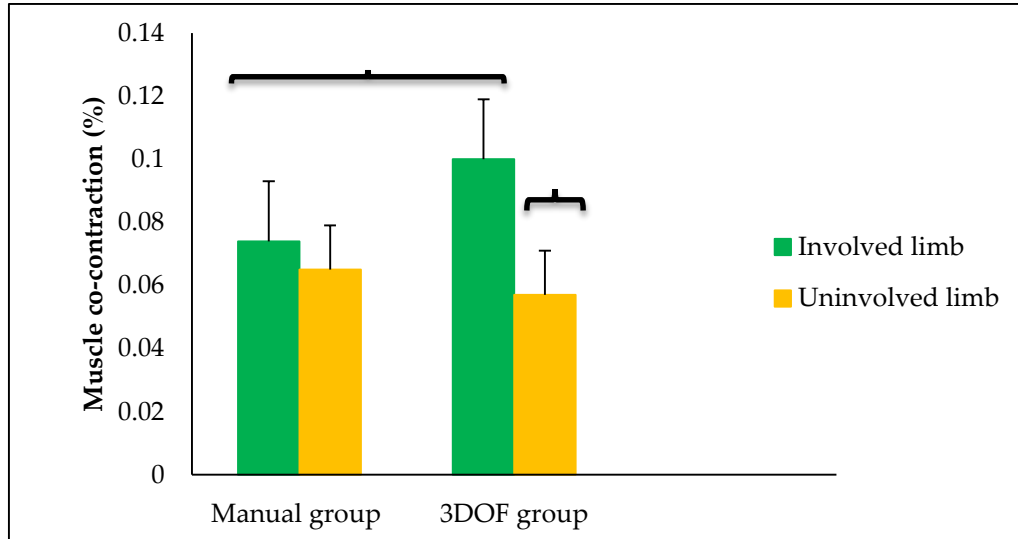


Figure 30 LG-VL muscle co-contraction during MS for involved and uninvolved limbs of 3DOF and manual groups (Mean (SD))

A Significant main effect of time was found in MG-VM muscle co-contraction index during TS with the muscle co-contraction index decreased significantly after training for both groups (pre-training: 0.055 ± 0.057 ; post-testing: 0.036 ± 0.02 ; $p=0.093$) (Figure 24). Significant main effect of limb was detected for MH-VM during WA ($p=0.002$) and MS ($p=0.003$), LH-VL during MS ($p=0.002$), and for MG-VM during MS ($p=0.008$) and TS ($p=0.007$) with the involved limb had significantly higher muscle co-contraction indexes compared to the uninvolved limb at pre and post-training testing sessions.

5.6.3 Correlation Between Muscle Co-contraction and Onset-to-Peak Muscle Activity

The length of onset-to-peak muscle activity of LH muscle at pre-training testing had a moderate to strong positive correlation with the pre-training muscle co-contraction indexes of LH-VL during WA ($r=0.427$, $p=0.088$) and during MS

($r=0.672$, $p=0.003$), LG-VL during MS ($r=0.532$, $p=0.028$). The length of onset-to-peak muscle activity of MG muscle at pre-training testing had a moderate positive correlation with the pre-training muscle co-contraction index of LG-VL during WA ($r=0.405$, $p=0.096$). The length of onset-to-peak muscle activity of SOL muscle at pre-training testing had a moderate negative correlation with the pre-training muscle co-contraction indexes of MG-VM during WA ($r=-0.454$, $p=0.077$) and MG-VM during TS ($r=-0.470$, $p=0.066$). Additionally, the length of onset-to-peak muscle activity of VL muscle at pre-training testing had a moderate positive correlation with the pre-training muscle co-contraction indexes of LG-VL during MS ($r=0.497$, $p=0.036$) and a strong correlation with muscle co-contraction of LH-VL during MS ($r=0.527$, $p=0.025$) and MH-VM during MS ($r=0.554$, $p=0.017$). The length of onset-to-peak muscle activity of VM muscle at pre-training testing had a moderate negative correlation with pre-training muscle co-contraction index of MG-VM during WA ($r=-0.476$, $p=0.046$).

The length of onset-to-peak muscle activity of LH muscle at post-training testing had a strong positive correlation with the post-training muscle co-contraction index of VL-LH during WA ($r=0.611$, $p=0.009$). The onset-to-peak muscle activity of LG muscle at post-training testing had a moderate positive correlation with the post-training muscle co-contraction index of LG-VL during WA ($r=0.485$, $p=0.048$) and moderate to strong negative correlations with VL-LH during TS ($r=-0.52$, $p=0.032$), MH-VM during TS ($r=-0.642$, $p=0.005$), LG-VL during TS ($r=-0.483$, $p=0.049$), and MG-VM during TS ($r=-0.634$, $p=0.006$). The onset-to-peak muscle activity of MG muscle at post-training testing had moderate to strong negative correlations with the post-training muscle co-contraction index of MH-VM during MS ($r=-0.656$, $p=0.003$),

MG-VM during MS ($r=-0.439$, $p=0.069$), and MG-VM during MS ($r=-0.597$, $p=0.009$). The onset-to-peak muscle activity of the VL muscle at post-training testing had moderate to strong negative correlations with post-training muscle co-contraction indexes of MH-VM during TS ($r=-0.446$, $p=0.073$) and with VL-LH during TS ($r=-0.579$, $p=0.015$). The onset-to-peak muscle activity of the VM muscle at post-training testing had moderate to strong positive correlations with post-training muscle co-contraction indexes of LH-VL during TS ($r=0.652$, $p=0.003$), ML-VL during TS ($r=0.552$, $p=0.018$), LG-VL during WA ($r=0.506$, $p=0.032$) and MS ($r=0.0456$; $p=0.057$), and TS ($r=0.0596$, $p=0.009$).

The change in onset-to-peak muscle activity of LH muscle between pre to post-training had moderate to strong positive correlations with post-training muscle co-contraction indexes of LG-VL during WA ($r=0.401$, $p=0.09$) and MG-VM during WA ($r=0.595$, $p=0.009$). The change in onset-to-peak muscle activity of VL muscle between pre to post-training had moderate to strong positive correlations with post-training muscle co-contraction indexes at post-training testing of VL-LH during TS ($r=0.789$, $p<0.001$), MH-VM during TS ($r=0.678$, $p=0.002$), LG-VL during WA ($r=0.415$, $p=0.087$) and during TS ($r=0.715$, $p=0.001$). In addition, the change in onset-to-peak muscle activity of VM muscle between pre to post-training had moderate positive correlation with post-training muscle co-contraction indexes of the LH-VL during TS ($r=0.447$, $p=0.063$), MH-VM during TS ($r=0.478$, $p=0.045$) and with LG-VL during TS ($r=0.414$, $p=0.087$).

5.7 Discussion

The purpose of this study was to investigate whether administration of mechanical perturbation training provides effects similar to manual perturbation

training on neuromuscular compensation including the length of onset-to-peak muscle activity and muscle co-contraction indexes and to determine how these compensations change after training. The results of this study revealed that both manual and mechanical perturbation training induce similar effects on neuromuscular compensation (time duration of onset-to-peak muscle activity and the magnitude of muscle co-contraction index). These findings were anticipated as the mechanical device provides perturbation stimuli similar to those of manual perturbation training. Additionally, the magnitudes of all perturbation stimuli parameters related to the amplitudes, velocities, accelerations, and directions were determined in our motion analysis laboratory during real-time manual perturbation training.

The results of this study showed that time duration of onset-to-peak muscle activity did not change in the quadriceps or hamstring for patients in both perturbation training. It might be due to the fact that the neuromuscular system of patients with ACL rupture adapts as a protective mechanism to prevent the occurrences of dynamic knee instability that are associated with both pain and fear¹⁰⁴. Additionally, it has been suggested that the ACL rupture causes alteration in the central nervous system organization and function¹⁶⁷⁻¹⁶⁹. Some studies suggested that the perturbation training may have an effect on the somatosensory and gamma loop functions¹⁶⁷⁻¹⁶⁹, but we do not know whether the perturbation training has an effect on the central motor programming of the nervous system. In this study we evaluated time duration between the onset-to-peak muscle activities, however, we did not evaluate whether there perturbation training caused alteration in the occurrence of onset-to-peak muscle activity time points during stance phase. It is possible that perturbation training induced reorganization to neuromuscular strategies including shifting (earlier or

delaying) in the occurrence of onset or peak muscle activity time points without changes in the time duration between onset-to-peak muscle activity. Hurd and colleagues reported that perturbation training caused a shift in the onset-to-peak muscle activity for MH from after to before heel strike⁵¹. Additionally, we investigated only the effect of perturbation training on the time duration from onset-to-peak muscle activity, but we did not evaluate the changes in the total duration of muscle activity (from turning on to turning off). In addition, we evaluated time duration from onset-to-peak muscle activity only during the stance phase of gait cycle, but not throughout gait cycle. There are some muscles turns on prior to the beginning of the stance phase. Further research might be needed to clarify whether the perturbation training induce changes in the total duration of muscle activity, from muscle turns-on to turns-off. In addition, future research may consider evaluating the effect of the perturbation training on the time duration from onset-to-peak muscle activity throughout full gait cycle.

The result of this study showed the 3DOF group had longer duration of onset-to-peak muscle activity for the LG and MG muscles compared to manual group. 3DOF group, however, demonstrated longer duration of onset-to-peak muscle activity in both the involved and uninvolved limbs for those muscles. The longer time duration of onset-to-peak muscle activity of 3DOF group might be due to the fact that 3DOF group having a mixed of patients with dynamic knee stability and dynamic knee instability while manual group having only patients with dynamic knee instability.

For MH muscle, the involved limb demonstrated longer muscle activity duration compared to the uninvolved limb regardless of the treatment group. This finding was not surprising after ACL rupture as most studies reported similar finding

where the hamstring muscle demonstrates prolonged muscle activity duration during the involved limb's stance phase of the gait cycle to provide knee stability^{12,47,157}.

The results of this study also show that administration of either manual or mechanical perturbation training provides similar effect on muscle co-contraction indexes in patients with ACL rupture during gait. Group by time by limb interaction was only found for LH-VL muscle co-contraction index during TS. This interaction resulted from an increase in the uninvolved limb LH-VL muscle co-contraction during TS of stance phase after training. Knowing that the uninvolved limb demonstrated significantly lower LH-VL muscle co-contraction during TS compared to the involved limb and compared to other muscle pairs. Additionally, only one muscle pair (LG-VL during WA) demonstrated different responds to manual and mechanical perturbation training with subjects who were trained on the mechanical device increased while the subjects who were trained manually increased their LG-VL muscle co-contraction during WA after training. This pattern was not consistent in other muscle pairs; therefore we cannot conclude from this finding that manual and mechanical perturbation training induce different effects on muscle co-contraction. The increased in muscle co-contraction in the 3DOF group may resulted from the increase demand on the joint during participation in dynamic functional activities which in turn increased the muscle activation to provide joint stability. After training, subjects improved their functional performance and scored higher on patient-reported knee function measures. As a result, subjects might start feeling more confident about their knee status and started to place more load during functional activity. Additionally, it may result from agility training that 5 subjects of 3DOF group received in addition to the perturbation training. In comparison, the decrease LH-VL muscle co-contraction

during WA in manual group may be due to the fact that the subjects in manual group were all patients with dynamic knee instability. Therefore they may adapted an abnormal neuromuscular strategies that are characterized by shifting their load toward the uninvolved limb due to the fear of loading the involved limb and to avoid the occurrence of knee giving ways that are associated with pain.

What was surprising is the uninvolved limb which demonstrated an increased in the muscle co-contraction for some muscle pairs after training. The magnitude of the muscle co-contraction indexes of the uninvolved limb before training was smaller compared to that of the involved limb. This small muscle co-contraction index in the uninvolved limb prior to training might indicate neuromuscular deficits. However we can determine whether these deficits existed before the injury or were caused by the ACL injury. The increase in the muscle co-contraction of the uninvolved limb might be reasonable as a group of patients would lean toward overusing the uninvolved limb due to the fear of loading the injured limb and to avoid the occurrence of knee giving ways. As a result to the shift in the loading mechanism from the involved limb to the uninvolved would place higher demand on the uninvolved knee and knee flexor and extensor respond by increasing the magnitude of muscle co-contraction to provide stability. The manual and mechanical perturbation programs included training techniques for both the involved and uninvolved limbs. Further, during the involved limb training patients respond by simultaneously contracting muscles of the uninvolved limb to stiffen joints and provide stability for the entire body. In turn, administration of perturbation training may have improved the neuromuscular responses that are manifested by increase the muscle co-contraction of the uninvolved limb. There is a growing evidence that healthy individuals exhibit neuromuscular

deficits especially among women¹⁷⁰⁻¹⁷³. Palmieri-Smith and colleagues reported that both healthy men and women individuals demonstrated imbalance between the medial and lateral quadriceps-hamstring muscle co-contraction with women demonstrated higher medial to lateral muscle co-contraction differences³⁹. Letafatkar and colleagues reported an increased in muscle co-contraction of healthy women who had a quadriceps dominance neuromuscular deficit after perturbation training¹⁷². Quadriceps dominance is described as an imbalance in the strength, coordination, and recruitment between the knee flexor and extensor with the hamstring muscle demonstrating a decrease in strength and activation¹⁷⁴. The decrease in strength and activity of the hamstring muscle compared to the quadriceps muscle may result in lower extremity injuries especially in athletic women. This neuromuscular imbalance between knee flexor and extensor is modifiable with appropriate interventions¹⁷⁴. The perturbation training might be a beneficial training that helps resolving neuromuscular deficit, restoring a balanced muscular activity between knee flexors and extensors, and improving knee dynamic stability^{36,51,172}. Therefore, these findings of lower muscle co-contraction in the uninvolved limb do not contradict with what is reported in the literature about increased muscle co-contraction in the involved limb of patients with ACL rupture.

The result of this study showed that subjects demonstrated a higher muscle co-contraction in the involved limb after training regardless of treatment group. The higher muscle co-contraction indicates an abnormal neuromuscular adaptation to stabilize the knee joint. The findings of this study contradict with what has been reported in other study that reported perturbation training reduce muscle co-contraction. Those previous studies analyzed their data based on patients' sex and

stability classification as they included only patient with dynamic knee stability. In this study we did not stratify the data based on patients' sex due to the small number of women and based on or stability classification as manual group included only patients with dynamic knee instability while the 3DOF group included a mixed of patients with dynamic knee stability and patient with dynamic knee instability. Patients with dynamic knee stability are those individuals who are able to resume preinjury activities level with no symptoms of dynamic knee instability for one year from the ACL injury^{8,12,147}. Patient with knee stability also walk with gait pattern similar to the healthy uninjured individuals^{35,52}. In comparison, patients with dynamic knee instability are patients who experience dynamic knee instability during simple daily activities^{7,8}.

The results of this study shows that the length of time duration of onset-to-peak muscle activity of quadriceps, hamstring, gastrocnemius, and soleus muscles had a moderate to strong relationship with the magnitude of muscle co-contraction of quadriceps-hamstring and quadriceps-gastrocnemius muscle pairs at both pre and post-training testing sessions throughout the stance phase of gait cycle. The directions of relationship were varied for different muscles based on anatomy and function of muscles. Additionally, the directions of relationships were varied from prior to post perturbation training. For some muscles, the length of time durations of onset-to-peak muscle activity associates with an increase the magnitude of muscle co-contraction. In contrast, the length of time duration of onset-to-peak muscle activity for other muscles associated with a decrease in the magnitude of muscle co-contraction.

There was a moderate to strong positive correlation between LH and the magnitude of muscle co-contraction for some muscle pairs prior and post-perturbation

training especially during WA and MS. This finding support the claim that knee flexor muscles respond by changing the pattern and duration of muscle activities to compensate for loss the passive constraint in the knee joint. Additionally, these findings go along with what has been reported in the literature that the changes in the knee flexor muscle activity accounts for the reduced knee external moments^{6,12,47,51,157}. This moderate to positive co-contraction of LH may suggest that hamstring contributes more than gastrocnemius muscle to stabilize the knee joint early in stance phase. The length of time duration of LH muscle associated with an LH-VL and LG-VL muscle co-contraction during WA and MS. This may account for preventing rotation motion of knee joint through balancing out the changes in rotation moment during both WA and MS^{39,175}. The changes in time duration of onset-to-peak muscle activity of LH muscle between pre and post-training testing had moderate to strong positive correlation with LG-VL and MG-VM muscle co-contraction during WA. The prolonged LH muscle activities may induce an abduction and rotation moments. In turn, the neuromuscular system responded by increasing LG-VL and MG-VM muscle co-contraction stabilize the tibia motion during WA interval.

The results of this study showed that SOL muscle demonstrated a reverse relationship with the magnitude of muscle co-contraction prior to training. The time duration of onset-to-peak muscle activity of SOL muscle had moderate negative correlation with muscle co-contraction of quadriceps-gastrocnemius muscle pairs. The negative correlations indicate that the longer the time duration of onset-to-peak muscle activity of SOL muscle is the smaller muscle co-contraction of quadriceps-gastrocnemius muscle pairs or vice versa. This finding may be related to the anatomy and function of the SOL muscle especially during weight-bearing activities (i.e.

walking).The SOL muscle does not cross the knee joint and it originates from the proximal tibia and contributes with other muscles in the ankle planter flexion. During the stance phase of walking, SOL muscle controls the anterior translation of tibia related to femur (ACL agonist muscle) when the foot is in contact with the ground. In the absence of the passive knee restraint (ACL rupture), SOL muscle limits the anterior displacement of the tibia, which in turn leads to decrease of muscle co-contraction (quadriceps and hamstring and quadriceps and gastrocnemius) to stabilize the knee joint¹⁷⁶.

Prior to perturbation training only MG of gastrocnemius muscle had a moderate positive relationship with muscle co-contraction of LG-VL during WA. After training, the time duration of both heads of gastrocnemius muscle activity had moderate to strong negative relationships with the magnitude of muscle co-contraction between quadriceps-hamstring and quadriceps-gastrocnemius muscle pairs especially during TS. The gastrocnemius muscle along with SOL muscle works as an ACL agonist that controls the anterior translation of the tibia. These finding may indicate that perturbation training has induced changes into the neuromuscular activation pattern of gastrocnemius muscle in attempt to provide dynamic knee stability during walking. Additionally, perturbation training may cause reorganizing in the activation pattern within the same muscle and between muscles. In this study, SOL muscle correlated negatively with muscle co-contraction prior to the training, however, this pattern was shifted to gastrocnemius muscle after perturbation training. Perturbation training may worked as a re-education training that enhance muscles' performance to provide dynamic stability^{36,51}. The time duration of gastrocnemius's muscle activity correlated with muscle co-contraction especially during TS interval of stance phase.

This might be true as increase in time duration from onset-to-peak muscle activity indicates that the peak muscle force of gastrocnemius does not occur till later of stance phase which is the time of TS. Therefore, gastrocnemius muscle generates force to control for the external moment that is applied onto knee joint during TS interval of stance phase. As a result, the increase in the time duration of onset-to-peak muscle activity decreases the demand on muscle co-contraction of quadriceps-hamstring and quadriceps-gastrocnemius muscle pairs to stabilize the knee joint during TS.

The time duration of onset-to-peak muscle activity of the VL muscle played a major role (found to be the most influential muscle) on muscle co-contraction. The onset time-to-peak muscle activity of the VL muscle prior to perturbation training had moderate to strong positive correlations with the muscle co-contraction of different muscle pairs. The concentric contraction of the VL muscle induces anterior displacement of the tibia during time interval during MS where the knee joint is preparing to start moving toward the straight position. Therefore, the time duration of onset-to-peak muscle activity of the VL increases the muscle co-contraction of LH-VL, LG-VL, and MH-VM to stabilize the knee joint. After perturbation training, the time duration of the VL muscle had a moderate to strong negative correlation with LH-VL and MH-VM during TS. These findings may indicate that the perturbation training induced a successful adaptation into the neuromuscular system. It has been reported that after rehabilitation, the VL muscle limits the internal rotation of the tibia as a protective mechanism even though the overall force of the quadriceps causes anterior displacement of the tibia¹⁵⁷. The adaptation in the VL muscle activity in controlling tibia internal rotation may explain the moderate to strong negative

correlation between onset-to-peak muscle activity of VL muscle and the muscle co-contraction of LH-VL and MH-VM during TS.

The length of time duration for VM muscle demonstrated moderate negative relationship with muscle co-contraction of MG-VM during WA. This finding may be reasonable as a delay in producing enough muscle in VM will decrease the magnitude of MG-VM muscle co-contraction during WA to balance out the external abduction moment placed on the knee joint during WA^{1,39}. After training, the length of time duration for VM demonstrated a moderate to strong positive correlation with muscle co-contractions of different muscle pairs especially during TS. These findings may indicate that concentric contraction of the VM muscle induces anterior displacement of the tibia during which in turn increases the muscle activity of knee flexor to stiffen the knee joint and to provide dynamic knee stability. The time duration of VM muscle activity indicates a delay in generation of muscle force till later in stance phase. In result, that led to increase the magnitude of muscle co-contraction during the time of TS to stabilize the knee joint against the anterior displacement induced by VM muscle.

While the changes in time duration of onset-to-peak muscle activity of VL and VM muscle between pre and post-training testing had moderate to strong positive correlation with LH-VL, MH-VM, and LG-VL muscle co-contraction during TS. The time duration of VL and VM muscles activities may induce an anterior tibia translation were encountered with an increase muscle co-contraction during TS to stabilize the tibia motion in the sagittal plane. The muscle co-contraction in the previously mentioned muscle pairs responded with an adequate muscle co-contraction to provide the stability to the anterior tibia translation caused by the concentric

contraction of the VL and VM muscles. It was noticeable that both quadriceps-hamstring and quadriceps-gastrocnemius muscles pairs contributed to the joint stability during the TS phase. It might be due to the fact that as the knee joint goes toward an extended position during the TS, the ability of the hamstrings to provide stability became less as angle of pull for the hamstrings becomes smaller ^{36,174,177}.

5.8 Limitation

The limitations of this study include usage of data from previous study for the manual group to serve as a comparison group however the researchers who conducted that study were well-trained and reliable for all of the manual perturbation training and clinical and motion analysis testing. The number of subjects in the 3DOF group is small, however, this study is a pilot study and findings of this study will allow us to design a powered study in the future. One limitation related to statistical analysis includes gender. It is well reported in the literature that women demonstrates higher neuromuscular deficit compared to their men counterpart and in their response to the perturbation training. Due to the small number of women participants in this study we did not include the gender in the statistical analysis of this study. One limitation is related to the training program as some of the subjects in 3DOF group received agility training while all subject in manual group did not receive the agility training. The onset time-to-peak muscle activity measure was analyzed during the stance phase of the gait cycle (100 ms prior to heel strike to Toe-off) where some of the muscles of interest were active prior to the stance phase. Therefore, onset time-to-peak muscle activity measure was not computed for some of the muscles, using full gait cycle will allow computing the onset-to-peak EMG time for all muscle of interest. In this study we did not evaluate whether perturbation training induced a shift in the time point of

muscle onset and peak muscle activity earlier or later during stance phase. Other limitation of this study is the variability of the EMG data among individual during walking trials. There was limitation that may be associated with training on the mechanical device as the therapist cannot physically sense whether the patient responses appropriately through selective muscle activation.

5.9 Conclusion

In conclusion, administering perturbation training using mechanical device provides effects similar to manual perturbation training on muscle activation timing and most of muscle co-contraction. The small ample size and the differences between groups (stability classification) may have affected the results of this study. Perturbation training attempts to resolve neuromuscular deficits and restore a balance in muscle activation between knee flexors and extensors to enhance the dynamic joint stability. Additionally, there was moderate to strong relationship between the time duration of onset-to-peak muscle activity and muscle co-contraction of quadriceps-hamstring and quadriceps-gastrocnemius muscle pairs at both the pre and post-training testing session. These relationships between time duration of muscles' activities and muscle co-contraction, regardless of the correlations' magnitudes and directions, may reflect the adaptations that take place in the neuromuscular system to provide dynamic knee stability.

Chapter 6

SUMMARY

6.1 Benefits of Using Return to Activity Criteria after ACLR

One goal of this work was to evaluate the effect of a battery of return to activity criteria testing to determine patients' readiness to return to participate in preinjury activities and to evaluate the ability of the return to activity criteria variables to predict return to participate in the same pre-injury activity level at 12-M and 24-M after ACLR. The novelty of using a comprehensive set of return to activity criteria measures is to allow clinicians to identify patients with poor knee function and limb movement asymmetry who might be at a high risk for secondary ACL injury after ACLR. In addition, the return to activity criteria may provide clinicians with cues on which patient can return to the same preinjury activity level in the near future based on performance-based and patients-reported measures early after the ACLR.

The other goal of this work was to evaluate the effectiveness of using automated device that provides mechanical perturbation training similar to the manual perturbation training. The mechanical device can generate multidirectional translation stimuli similar to that of manual perturbation training. The mechanical perturbation device may be beneficial to restore normal knee mechanics, knee functional performance, and to improve the dynamic knee stability in patients with an ACL rupture. Inventing automated device that provides controlled and standardized perturbation stimuli may facilitate the use of the perturbation training in a wider range among the rehabilitation clinics to standardize the ACL rehabilitation programs. Furthermore, implementing an automated device that provide mechanical perturbation

training in rehabilitation clinics will reduce the extensive labor work and the time period of the treating therapist without affecting the patients outcomes.

6.2 Aim 1 Findings

Aim 1 of this dissertation was to investigate patients' functional performance-based and patient-reported measures at 12 and 24 months after ACLR between those patients who passed (PASS) and those who failed (FAIL) RTAC at 6-M after ACLR and how their functional performance changes over time.

Hypotheses 1.1: Subjects who PASS RTAC at 6-M after ACLR will PASS RTAC at 12-M and 24-M after ACLR, while subjects who FAIL on RTAC at 6-M after ACLR will continue to FAIL RTAC by demonstrating poor knee function performance and limb movement asymmetry at 12-M and 24-M after ACLR.

Hypotheses 1.2: The FAIL group will demonstrate greater improvements in performance-based measures compared to the PASS group between the period of 6-M to 12-M and 12-M to 24-M after ACLR with the greatest improvement occurring during the first year after ACLR.

Hypotheses 1.3: The FAIL group will demonstrate greater improvements in patient-reported measures compared to the PASS group between the period of 6-M to 12-M and 12-M to 24-M after ACLR with the greatest improvement occurring during the first year after ACLR.

The results of this first aim supported these hypotheses. Three-quarters of subjects who had passed RTAC at 6-M after ACLR demonstrated normal knee function and normal knee movement symmetry at 12-M and 24-M after ACLR. In comparison, one half to two-third of the subjects who failed on RTAC at 6-M after ACLR demonstrated poor knee function and limb-to-limb movement asymmetry at

12-M and 24-M respectively after ACLR. Subjects who passed RTAC 6-M after ACLR were two times more likely to PASS RTAC again at 12-M and 24-M after ACLR than those who failed, while those subjects who failed on RTAC 6-M after ACLR were 2.7 and 1.72 times more likely to fail on RTAC again at 12-M and 24-M respectively after ACLR than those who passed.

FAIL group improved their scores on knee performance-based and patient-reported measures between 6-M and 12-M follow-up testing after ACLR, and continued to improve 24-M after ACLR. FAIL group demonstrated the greatest improvement on all of performance-based and patient-reported measures between 6-M and 12-M interval after ACLR, except for KOS-ADLS. The KOS-ADLS scores for both groups did not change over time as this particular measure asks questions related to basic daily living activities that are performed by most subjects with no difficulties.

The results of this study highlight the importance of using a battery of return to activity criteria to identify those patients with strength deficit, neuromuscular dysfunction, and limb-to-limb functional asymmetry early after ACLR. This in turn will help clinicians providing an extended rehabilitation programs to resolve patients' functional limitation and restore normal movement symmetry before they are cleared to begin participation in highly physical activities. Additionally, the result of this study would facilitate a safe return to participate in the preinjury activity level with minimum to no risk of second ACL injuries. The large number of subjects with poor knee functional performance and limb movement asymmetry that were classified as FAIL on RTAC may explain the variability of outcomes and the poor the rate of return to the preinjury activity level after ACLR. To this end, the result of this work shows the importance of utilizing a criterion-based approach using a comprehensive set of

objective criteria in the rehabilitation clinics to clear patient to return to their preinjury activity level.

6.3 Aim 2 Findings

The prediction of return to preinjury activity level has been estimated using only explanatory variables that include patient demographics, concomitant injuries, and treatment variables. Aim 2 of this dissertation was to investigate whether RTAC variables at 6-M after ACLR predict return to participate in the same preinjury activity level 12-M and 24-M after ACLR and to investigate which combination of RTAC variables 6-M after ACLR predicts return to participate in the same preinjury activity levels 12-M and 24-M after ACLR.

Hypotheses 2.1: Subjects who PASS RTAC at 6-M after ACLR are more likely to return to participate in the same preinjury activity level at 12-M and 24-M after ACLR while subjects who FAIL RTAC at 6-M after ACLR are more likely not to return to the same preinjury activity level at 12-M and 24-M after ACLR.

Hypotheses 2.2: RTAC variables will predict return to participate in the same preinjury activity level at 12-M and 24-M after ACLR.

Hypotheses 2.3: A combination of functional performance and patient-reported measures will explain a large portion of variance of return to participate in the same preinjury activity level at 12-M after ACLR.

Hypotheses 2.4: A combination of functional performance measures will explain a larger portion of the variance of return to participate in the same preinjury activity level 24-M after ACLR.

The results of this second aim supported these hypotheses. Eighty-one percent of those who PASS RTAC at 6-M return to participate in the same preinjury activity

level while 44.2% of those who FAIL on the criteria at 6-M returned to participate in the same preinjury activity level at 12-M after ACLR. Further, 84.4% of those who PASS RTAC at 6-M after ACLR returned to participate in the same preinjury activity level while 46.4% of those who FAIL on RTAC returned to participate in the same preinjury activity level 24-M after ACLR.

The results of aim 2 show that individual RTAC variables can predict return to the same preinjury activity level at both 12-M and 24-M after ACLR. Further, the combination of performance-based and patient-reported measures of the RTAC variables contributed to the ability of prediction of the return to the same preinjury activity level at 12-M after ACLR and explained one-quarter of the outcome variance. Only the performance-based measures of RTAC variables, however, contributed to the ability of the prediction of the return to participate in the same preinjury activity level at 24-M after ACLR and explained more than one third of the outcome variance.

The rates of return to the preinjury activity level at 12-M and 24-M were superior to those reported in the literature which might be due to the use of RTAC criteria. Utilizing a comprehensive set of RTAC that encompasses both performance-based and patient reported measures can successfully determine the patients' readiness to return to their preinjury activity level. Additionally, utilizing a battery of RTAC testing helps clinicians to identify which patient can resume preinjury activity level 12-M and 24-M after surgery based on their knee functional performance and limb movement symmetry. The RTAC also assist clinicians to identify those patients who continue to exhibit functional limitation and who may require an extended rehabilitation training including quadriceps strength, plyometric, and neuromuscular training to resolve their functional limitations.

The result of aim 2 of this dissertation is the first study to use factors related to the patients' functional performance and patient-reported to predict the return to the same preinjury activity level at 12-M and 24-M after ACLR. The results of this study allow clinicians to identify patients who are more likely to return to participate to the same preinjury activity level 12-M and 24-M after ACLR. In addition, to identify patients with functional deficit who are most likely will not return to participate in the same preinjury activity level 12-M and 24-M after ACLR.

The combinations of RTAC variables were able to explain one-third to one-fourth of variance of the return to the same preinjury activity level at 12-M and 24-M respectively after ACLR. In this aim we used a patient-reported variable related to activities of daily living, KOS-ADLS, instead of using variables related to sport activities to predict returning to preinjury activity level. The RTAC, however, were originally instituted to assess patients' knee functional performance and limb movement symmetry during basic functional tasks. Investigating variables related to participation in sport activities, may contribute to the ability of explaining the variance of the return to the same preinjury activity level.

6.4 Aim 3 Findings

Manual perturbation training is a type of neuromuscular training and it has been advocated to mitigate abnormal gait pattern and improve dynamic knee stability and function of patients with ACL rupture. Perturbation training is not widely used as part of the ACL rehabilitation program in the United States. Further, the perturbation training requires extensive physical labor and one-on-one time from the treating therapist. It is unknown whether administering perturbation training using mechanical

device provides effects similar to manual perturbation training on knee mechanics and functional performance of patients with acute ACL rupture.

Aim 3. To evaluate whether administration of 10-training sessions of mechanical perturbation training using 3DOF plate provides effects similar to 10-training sessions of manual perturbation training on gait mechanics, functional performance-based, and patient-reported measures in patients with acute unilateral ACL injury.

Hypothesis 3.1: Subjects who receive 10-training sessions of mechanical perturbation training using the 3DOF plate will demonstrate knee kinematics similar to those subjects who receive 10-training sessions of manual perturbation training at post-training testing session.

Hypothesis 3.2: Subjects who receive 10-training sessions of mechanical perturbation training using the 3DOF plate will demonstrate knee kinetic similar to those subjects who receive 10-training sessions manual perturbation training.

Hypothesis 3.3: Subjects who are trained on the 3DOF plate will be equally likely to PASS RTAC compared to subjects who are trained on the manual perturbation training.

Hypothesis 3.4: Subjects who are trained on the 3DOF plate will improve their performance-based and patient-reported measures similar to those subjects who receive manual perturbation training.

The results of the third aim of this study supported these hypotheses. The gait motion analysis and clinical testing revealed that administering perturbation training using mechanical device provides effects similar to manual perturbation training on knee kinematic and kinetic, performance-based, and patient-reported measures.

The clinical testing demonstrated that subjects who received perturbation training using mechanical device did not differ from those who received manual perturbation training. Additionally, subjects in both groups demonstrated similar improvement in the performance-based and patient-reported measures after training. The third hypothesis of this study was not supported as two subjects from 3DOF group passed RTAC after perturbation training while no subject from the manual passed the criteria. This finding does not support our hypothesis that patients who are trained on the 3DOF plate will be equally likely to pass return to activity criteria compared to subjects who are trained on the manual perturbation training. The underlining difference in stability classification between groups may account for this finding as 3DOF group included 6 subjects with dynamic knee stability compared to manual group whom included only subjects with dynamic knee instability. Therefore, 3DOF group had better chance to pass RTAC after perturbation training.

6.5 Aim 4 Findings

The neuromuscular maladaptation is commonly seen in patients with ACL rupture. Patients adapt increase in the magnitude of muscle co-contraction between knee flexion and extensor muscles to stabilize the knee joint. Additionally, there are corresponding changes in the timing duration of knee flexor muscles activity. The manual perturbation training has been shown to be an effective intervention that reduces muscle co-contraction and improve the dynamic knee stability. The effect of using automated device that provide similar perturbation translations similar to the manual perturbation training on the neuromuscular strategies has not been investigated.

Aim 4. To investigate whether administration of mechanical perturbation training using the 3DOF plate provides similar effects as using manual perturbation on muscle activation time and muscle co-contraction measures in athletes with ACL rupture.

Hypotheses 4.1: Subjects who are trained on the 3DOF will demonstrate a reduction in muscle co-contraction indexes on the involved limb, similar to subjects who are trained on the manual perturbation training at post-training testing session compared to pre-training testing.

Hypotheses 4.2: Subjects who are trained on the 3DOF will demonstrate short duration of onset time-to-peak muscle activity for hamstring, gastrocnemius, and soleus muscles similar to those who are trained on the manual perturbation training at post-training testing session compared to the pre-training testing.

Hypotheses 4.3: The length of onset time-to-peak muscle activity will positively correlate with the muscle co-contraction indices at post-training testing session, and pre to post-training change in onset time-to-peak muscle activity will negatively correlate with the muscle co-contraction of the hamstring, gastrocnemius, and soleus muscles at post-training testing session in manual and 3DOF groups.

The results of this fourth aim partially supported these hypotheses. Administering perturbation training using mechanical device provides effects similar to the manual perturbation training on the onset-to-peak muscle activity and most muscle co-contraction indexes. There were a couple of different muscle co-contraction responses to the perturbation training with the 3DOF group demonstrated an increase in muscle co-contraction. However, these responses were not consistent among other

muscle pairs. The increased in 3DOF's muscle co-contraction may resulted from the differences in the subjects stability classification as the 3DOF included a mixed of subjects with dynamic knee stability (n=6) and dynamic knee instability while the manual group includes only subjects with dynamic knee instability. Additionally, 5 subjects in the 3DOF group received agility training while the subjects in the manual group did not receive agility training. The results of this aim shown also that there is a weak to strong relationship between the muscle co-contraction of quadriceps-hamstring and quadriceps-gastrocnemius muscles pairs and the time duration from onset-to-peak muscle activity at both the pre and post-training testing session. Additionally, the changes in time duration from onset-to-peak muscle activity caused by the perturbation training have a weak to strong relationship with the muscle co-contraction of quadriceps-hamstring and quadriceps-gastrocnemius muscle pairs at the post-training testing session. The relationships between the time duration from onset-to-peak muscle activity and the muscle co-contraction indexes may improve the dynamic knee stability, enhance the neuromuscular integration, and coordination during participation in function activities of patients with ACL rupture.

The overall goal of this proposal is to improve patients' functional outcomes and their ability to return to activities after ACLR by using a battery of RTAC that can determine patients' readiness to return to preinjury activity level. The RTAC includes a comprehensive set of performance-based and patient-reported measures that are capable to identify patients with knee function deficit and limb movement asymmetry early after ACLR or after an extended period of time after ACLR. In this study, we also used prediction methods that allow clinicians to identify which athletes can return to their actives based on their functional performance measures early after surgery.

The result of this study will allow clinicians to identify patients who will not return to participate in the same preinjury activity level 12-M and 24-M after ACLR. Therefore, implementing RTAC in rehabilitation clinics will allow clinicians also to identify patients with abnormal knee function and limb-to-limb asymmetry that require additional training to address functional deficits and movement asymmetry before allowing these patients to return to their preinjury activities. The results of this study revealed that RTAC variables contributed to the ability of predicting return to participate in the same preinjury activity level at midterm and long term after ACLR. Our RTAC are comprehensive as they encompass both functional performance tests that replicate the demands of on field performance of sport activities including jumping, cutting, pivoting, taking-off, and landing maneuvers^{64,80,81}.

In addition these tests are typically quickly administered, require little equipment to perform, and allow for consistent comparison between the involved and uninvolved limbs; which are ideal for both clinical and research evaluations. Patient-reported measures are also easy to administer and provide valuable information about knee function and how knee symptoms affect the patient's ability to perform daily living activities.

In addition, the goal of this study was to also improve the knee functionality and restore normal movement symmetry of athletes with ACL rupture through interventions using technological devices. For patients who choose non-surgical management or delayed ACLR surgery, incorporation of a low-cost mechanical perturbation device into the rehabilitation program was beneficial in improving knee function and restore normal knee mechanics. The results of this study shown that incorporating a perturbation training using mechanical device that provides

multidirectional translation was effective to improve knee stability, knee mechanics, and functional performance of patient with an ACL rupture. Furthermore, mechanical perturbation training may replace the manual perturbation training as it can reduce the extensive physical labor and the amount of time that a therapist needs to treat a single patient in a clinical rehabilitation setting. The automated platform device is commercially viable, cost-effective, controllable, and clinically relevant testing device that can also be used in research settings.

6.6 Future Work

Further work is need to evaluate whether FAIL group who demonstrated poor knee function and limb movement asymmetry will have higher incidence of second ACL injury in the short and long-term after reconstruction surgery compared to those with normal knee function and limb movement symmetry. In addition, to investigate whether FAIL group will develop radiological signs of knee osteoarthritis after ACLR compared to those patients with normal knee function and movement symmetry. Di Stasi and colleague investigated the gait pattern differences between those who PASS and FAIL on the RTAC at 6-M after ACLR⁹⁶. Di Stasi's study found that the PASS group had less movement asymmetry during walking compared to those who FAIL⁹⁶.

The factors related to the patient-reported measures were successful to explain the variance of return to participate in the same preinjury activity level at one year but not at two year after surgery. Future work may consider investigate the return to participate in the same preinjury activity level using factors related to participation in sport activities (i.e. ACL-return to sport after injury (ACL-RSI) and International Knee Documentation Committee 2000 Subjective Knee Form (IKDC2000)).

Future work is needed to evaluate the effect of an extended number of perturbation training sessions (manual or mechanical) on the limb-to-limb gait asymmetries. Further, to evaluate the effect of mechanical perturbation training on returning to the preinjury activity level of patients with ACL rupture.

The manual perturbation training has been shown to restore balanced quadriceps-hamstring muscle activation in healthy women individuals^{51,172}. The effect of mechanical perturbation training as a prevention training is to be determined.

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Appendix A

THE 3DOF MECHANICAL PERTURBATION TRAINING PROGRAM

Appendix A: The 3DOF Mechanical Perturbation Training Program			
	Early (Estimated Treatment 1-3)	Middle (Estimated Treatment 4-7)	Late (Estimated Treatment 8-10)
Anterior/Posterior and Medial/Lateral 3DOF platform	Position: Patient on board (bilateral 1st treatment, progress to unilateral) — Eyes straight ahead Application: Inform the patient of direction and timing of rollerboard movement — Slow application of force, Low magnitude, — Straight plane of movement (do all A/P reps before you begin M/L) Observe: Cue patient to avoid massive co-contraction at knee — Do not overstress beyond limit of stability (don't induce fall)	Position: Unilateral (avoid forefoot abduction/adduction) Application: Unexpected forces — Rapid increasing magnitude force application — Add rotation and diagonal motions — Alternate plane of movement (start A/P, then M/L, progress to A/L/IR) — Short delay between subsequent force applications Distraction: May begin to add distraction (ball toss, stick work) Observe: Observe difficulty with recovery but few to no falls	Position: Unilateral Application: Increased magnitude of force application — Random direction movements — Little to no delay between applications Distraction: Increase speed and magnitude of distraction — Consider sport specific positions Observe: Look for disassociation of hip, knee, and ankle

<p>3DOF platform and Stationary Platform</p>	<p>Position: One foot on the rollerboard, one on the platform</p> <ul style="list-style-type: none"> – Eyes straight ahead, equal weightbearing on both lower extremities <p>Application: Inform patient of direction and timing of movement</p> <ul style="list-style-type: none"> – Slow application of force, low magnitude – All directions A/P, M/L, IR/ER, diagonals <p>Observe: Cue patient to maintain equal weightbearing bilaterally (watch for unweighting of the involved limb as level of difficulty increases)</p> <ul style="list-style-type: none"> – Do not overpower the patient, board should not move > 1 or 2 inches – Match therapist’s forces w/o excessive movement of roller board 	<p>Position: One foot on the rollerboard, one on the platform</p> <ul style="list-style-type: none"> – Eyes straight ahead, equal weightbearing on both lower extremities <p>Application: Unexpected forces</p> <ul style="list-style-type: none"> – Rapid, increasing magnitude force application – Begin combining directional movements (Ant with IR) <p>Distraction: May begin to add distraction (ball toss, stick work)</p> <p>Observe: Cue patient to maintain equal weightbearing bilaterally (watch for unweighting of the involved limb as difficulty level increases)</p> <ul style="list-style-type: none"> – Do not overpower the patient, board should not move > 1 or 2 inches – Cue patient to react as you remove force (avoid rebound board movement) 	<p>Position: One foot on the rollerboard, one on the platform</p> <ul style="list-style-type: none"> – Eyes straight ahead, equal weightbearing on both lower extremities <p>Application: Increased magnitude force application</p> <ul style="list-style-type: none"> – Random direction movements – Little to no delay between applications <p>Distraction: Increase speed and magnitude of distraction</p> <ul style="list-style-type: none"> – Consider diagonal/sport specific stance (forward split, backward split) <p>Observe: Cue patient to maintain equal weight bearing bilaterally (watch for unweighting of the involved limb as difficulty level increases)</p> <ul style="list-style-type: none"> – Cue patient to react as you remove force (avoid rebound board movement)
<p>3DOF platform and Stationary Platform instructions: Setup: The involved leg is placed on either the 3DOF platform or the stationary platform and after 3 sets of 1 minute, the legs are alternated and the treatment is repeated Instructions: <i>Meet the force, Don't beat the force.</i> “When the platform moves, resist the exact movement in speed and magnitude. Do not try to overpower the platform.”</p>			
<p>COMMON THEMES IN PERTURBATION TRAINING</p>			
<p>Tools: Simbex device and Sport Specific Equipment Progressions: Vary by individual, estimates are noted above</p>		<p>Time: 3 sets of 1 minute of each, rest time for calf stretching as needed Phases: 10 treatments total</p>	
<p>Application to Surface - As the stress to the patient increases in one area (i.e. change force application from expected to unexpected), the intensity of another application variable (i.e. magnitude of speed) must decrease. Once the patient is successful, progress toward resumption of altered variable (magnitude or speed) Distraction of Patient - When progressing a patient in difficulty level or progressing to the next phase of training, the distraction level for 1 or 2 treatments may need to be decreased until the patient's skill level has improved. Once the patient is successful, progress toward resumption of the previous level of distraction and progress. Observation of Patient- Each time stress is added to the training program (by application or distraction) you may see a decrease in performance level. This will require more cueing and feedback until the new skill is acquired and more stress can be incorporated.</p>			

Appendix B

INSTITUTIONAL REVIEW BOARD APPROVAL

B.1 LETTER OF APPROVAL



RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
Ph: 302/831-2136
Fax: 302/831-2828

DATE: February 12, 2014

TO: Lynn Snyder-Mackler, PT, ScD, FAPTA
FROM: University of Delaware IRB

STUDY TITLE: [535813-1] Reactive Agility System for ACL Rehabilitation

SUBMISSION TYPE: New Project

ACTION: APPROVED
APPROVAL DATE: February 12, 2014
EXPIRATION DATE: December 17, 2014
REVIEW TYPE: Full Committee Review

Thank you for your submission of New Project materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Nicole Farnese-McFarlane at (302) 831-1119 or nicolefm@udel.edu. Please include your study title and reference number in all correspondence with this office.