ABSTRACT

CARDIOVASCULAR HEALTH OF INDIVIDUALS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

By

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Previous literature has indicated that individuals with a history of anterior cruciate ligament reconstruction (ACLR) are less likely to be active, may experience negative changes in weight status, and may have reduced cardiorespiratory fitness (CRF) following surgery as compared to uninjured individuals. Despite the key role of physical activity (PA), obesity, and CRF in the prevention of noncommunicable diseases; it is unclear how these factors change in a population of young individuals who have experienced a period of reduced activity during rehabilitation for a traumatic knee injury. The overarching aim of this dissertation was to characterize cardiovascular health risk factors such as PA, BMI, body composition, CRF, and arterial stiffness as measured by carotid-to-femoral pulse wave velocity (cfPWV) and understand how these variables change throughout recovery from ACLR.

This dissertation is comprised of three studies. First, PA was measured at 6- and 9-months post-surgery in adolescent individuals with a history of ACLR. No differences were observed in moderate-to-vigorous PA volume, but individuals with ACLR had lower daily step counts than their uninjured peers. There was also no change in PA from 6 to 9 months for adolescents with ACLR. Uninjured individuals were no more likely to meet PA recommendations for MVPA and step counts than individuals with ACLR at 6 months and 9 months.
Second, a retrospective chart review was conducted to examine change in BMI of adolescents and adults from pre-surgery to 6 months post-ACLR. Adolescent and adult participants experienced a significant increase in body mass and BMI from pre- to 6 months post-ACLR.

Lastly, an exploratory study was conducted to evaluate cardiovascular health characteristics of individuals with a history of ACLR as compared to their uninjured peers. Body composition, CRF, arterial stiffness, and PA engagement was compared between young individuals with ACLR and uninjured controls. We observed that individuals with ACLR displayed similar characteristics of cardiovascular health as their uninjured peers, but those with ACLR may experience elevated BMI and fat mass and end a maximal graded exercise test sooner.

Taken together, these studies highlight health-related risk factors that should be addressed in adolescents and adults with a history of ACLR. The potential for reduced PA and undesirable changes to BMI and weight status are concerning in these otherwise healthy young individuals. The time following ACLR presents an opportunity for researchers and clinicians to promote healthy behaviors and these results also demonstrate the continued need for consideration of PA and diet during clinical care in order to minimize potential negative long-term effects of weight gain following surgery and ensure that ACLR does not become a risk factor for cardiovascular disease (CVD).
This dissertation is dedicated to my family and friends. You have provided me with the encouragement, love, and support through everything.
ACKNOWLEDGEMENTS

First, I would like to acknowledge my advisor Chris Kuenze for all of his support and guidance throughout my time in the Athletic Injury and Rehabilitation Lab at Michigan State University. Chris has consistently supported me professionally and personally and his encouragement to pursue my goals has been unmatched. I would not be where I am today without your mentorship and the time you have invested in me. I also would like to acknowledge my dissertation committee member and Master’s advisor Jim Pivarnik and his wife Linda. I cannot thank you both enough for all that you have done for me. I truly appreciate your encouragement, support, and dedication over the years. Additionally, thank you to the other members of my dissertation committee, Katharine Currie and Luke Wilcox. Your support, guidance, and the expertise you have provided throughout my dissertation have been paramount in the completion of this project. Thank you for the time you have dedicated to meeting with me and providing feedback on my dissertation. Thank you to the other graduate students, medical students, and undergraduate research assistants who have volunteered their time to help me execute data collection and gain mentoring experience. Finally, I would like to acknowledge my friends in the Athletic Injury and Rehabilitation Lab, Human Energy Research Lab, Department of Kinesiology, and Lansing area soccer community. Thank you for your friendship, support, and collaboration. I will never forget all of the good times we have shared over the years.
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CHAPTER 1: INTRODUCTION
STATEMENT OF THE PROBLEM

History of anterior cruciate ligament (ACL) reconstruction (ACLR) has detrimental effects on physical activity (PA) participation in the years following surgery.\textsuperscript{1–3} It is well established that physical inactivity can result in negative changes in BMI, body composition, cardiorespiratory fitness (CRF), and long-term cardiovascular health. With rates of ACLR having increased over 60% in the last 20 years among individuals under 30 years of age,\textsuperscript{4,5} it is crucial that we consider how this surgical procedure and the period of reduced recreational PA that is associated with rehabilitation may affect cardiovascular health in young and otherwise healthy individuals. Throughout rehabilitation there are evidence-based guidelines and goals associated with each phase, but cardiovascular conditioning focused on regaining CRF is not heavily emphasized.\textsuperscript{6,7} For the average patient who plans to return to recreational activity after the completion of rehabilitation, PA duration and intensity are often limited during rehabilitation and the patient is typically given little guidance for how to determine PA volume when returning to activity outside of the outpatient physical therapy setting. Lack of focus on regaining CRF and progressively increasing PA volume following surgery may have longer term implications for cardiovascular health. We do not yet fully understand how these risk factors may be impacted by a musculoskeletal surgical procedure such as ACLR and the ensuing rehabilitation process. Therefore, there is a critical need to characterize these health outcomes following ACLR to understand how modifiable risk factors may contribute to the potential development of cardiovascular disease morbidity and to address potential interventions in young individuals with ACLR.
STATEMENT OF THE PURPOSE

It is essential to characterize cardiovascular health-related risk factors in individuals with ACLR to determine potential risk of negative long-term health outcomes and identify intervention strategies to mitigate these sources of risk. There are a limited number of studies focusing on cardiovascular health and PA participation following surgery and even less reporting accelerometer-based assessments of PA in this population.\textsuperscript{1,2,8,9} As a result, it is unclear how changes in PA affect BMI, body composition, CRF, and other measures of cardiovascular health such as arterial stiffness in the short- and long-term following surgery and rehabilitation. Therefore, the purposes of this dissertation are threefold: 1) to evaluate change in PA among adolescent individuals from 6 to 9 months following ACLR as compared to healthy peers, 2) to evaluate change in body weight and BMI in adults and adolescents from pre-surgery to 6 months post-ACLR, and finally 3) to evaluate and compare PA engagement, body composition, CRF, and arterial stiffness of individuals within 6 years of ACLR and healthy age- and activity-level matched control individuals.
MANUSCRIPT 1 RESEARCH QUESTIONS AND HYPOTHESES

**Primary Purpose:** The primary purpose of study one is to compare moderate-to-vigorous PA (MVPA) time and step counts between adolescent individuals with and without a history of ACLR at 6- and 9-months following surgery.

   H 1.1. The primary hypothesis is that adolescents with ACLR will have less time spent in MVPA and fewer steps per day than their uninjured peers at each time point.

**Secondary Purpose:** The secondary purpose of study one is to evaluate MVPA and step count change in adolescents with ACLR from 6 to 9 months following surgery.

   H 1.2: The secondary hypothesis is that MVPA time and step count will increase from 6 to 9 months following surgery in the ACLR group.
MANUSCRIPT 2 RESEARCH QUESTIONS AND HYPOTHESES

Primary Purpose: The purpose of study two is to assess change in body weight and BMI from pre-surgery to 6 months post-ACLR in adolescent and adult patients with primary, unilateral ACLR.

H 2.1. The primary hypothesis is that absolute body weight and absolute BMI will significantly increase from pre- to 6 months post-ACLR in a similar magnitude for both adolescent and adult patients.
Primary Purpose: The primary purpose of study three is to characterize and compare body composition, cardiorespiratory fitness (CRF), device-measured PA, and carotid-to-femoral pulse wave velocity (cfPWV) (arterial stiffness) between individuals with a history of ACLR and uninjured, matched control participants with no history of lower extremity injury.

H 3.1: Individuals with a history of ACLR will have poorer indicators of cardiovascular health: greater percent body fat, lower CRF, lesser step counts and weekly MVPA time, and increased arterial stiffness.
SIGNIFICANCE OF THE STUDY

ACL injury and ACLR often occurs in healthy, active individuals early in the lifespan. There is preliminary evidence that individuals are less physically active after ACLR and that ACLR may negatively impact BMI, body composition, and CRF.\textsuperscript{1–3,9–12} However, there has not been a well-designed study that has attempted to comprehensively characterize the effects of ACLR on indicators of cardiovascular health. Successful completion of this dissertation will provide a multifaceted and novel characterization of cardiovascular health of individuals returning to activity post-ACLR. In study one we will contribute to the existing literature of PA patterns following ACLR with device-measured PA of an adolescent population at two timepoints following surgery. In study two we will expand on the limited knowledge of changes in body weight and BMI from pre-surgery to post-ACLR in both adolescent and adult patients with ACLR. Lastly, in study three we will explore the effects of ACLR on risk factors for cardiovascular disease. These factors will include body composition, device-measured PA, CRF profile (including lactate and BP variables), and arterial stiffness; all of which are relatively unknown in non-elite athletes with a history of ACLR.

The proposed projects are innovative because results from this dissertation will provide insight into the cardiovascular disease risk factor levels and potential for future metabolic consequences that may exist after individuals with ACLR have been cleared to return to activity. Excessive body weight and BMI, excessive body fat, increased arterial stiffness, and physical inactivity are risk factors for chronic disease and premature mortality. In addition to traditional risk factors associated with cardiovascular disease, evidence now suggests that poor CRF may be a stronger predictor of adverse
cardiovascular outcomes than these risk factors. Therefore, the proposed study will be among the first to develop our knowledge regarding the potential health consequences experienced by individuals who have undergone ACLR. Findings from this research could assist in the development of patient-centered education and evidence-based recommendations for introducing cardiovascular exercise training in addition to musculoskeletal training during rehabilitation following ACLR. Collectively, this information may also be used to inform and implement cardiovascular exercise interventions following release from formal rehabilitation prior to reengagement in sport. There are recommendations that volume of activity and athletic exposures should be modified, but a clear protocol for reintegrating high intensity, regular cardiovascular exercise has not been outlined for recreationally active individuals post-ACLR. Integration of cardiovascular exercise along with promotion of adequate PA and alternative PA modalities will also allow individuals to overcome barriers associated with PA in the years following ACLR that may mitigate potential risk of poor long-term cardiovascular health outcomes.
CHAPTER 2: REVIEW OF LITERATURE
This literature review explores the evidence regarding risk factors impacting cardiovascular health and the techniques used to measure these factors in individuals with and without a history of anterior cruciate ligament injury and surgical reconstruction.

**EPIDEMIOLOGY OF ACL INJURY AND ACLR**

**ANTERIOR CRUCIATE LIGAMENT ANATOMY**

The femur, tibia, and patella bones articulate to form the tibiofemoral joint (knee joint) and the patellofemoral joint. The tibiofemoral joint is a synovial, modified hinge joint that moves through flexion, extension, and a small degree of internal and external rotation. The knee joint gains its stability through the anterior cruciate (ACL) and posterior cruciate ligaments (PCL) (intra-articular ligaments), the medial collateral (MCL) and lateral collateral ligaments (LCL) (extra-articular ligaments), and a synovial joint capsule. Within the knee joint, fibrocartilage structures called menisci are located superiorly to the tibia to aid in absorption of compressive forces for the knee joint. The meniscus is divided into a crescent shaped medial meniscus and oval shaped lateral meniscus. The vascularity of the meniscus tissue varies throughout with the outer portion of the meniscus receiving the greatest blood flow and the inner portion of the meniscus receiving little to no blood flow.

One of the most commonly injured structures in the knee is the ACL. The ACL is a band of dense connective tissue most commonly divided into anteromedial (AM) and posterolateral (PL) bundles that originate from the medial portion of the lateral femoral
condyle and insert on the intercondylar tibial eminence. More recently a third bundle, the intermediate (IM) bundle has been identified along with its attachment sites. The bundles originate from the medial portion of the lateral femoral condyle and insert on the intercondylar tibial eminence. As the knee moves through flexion, the AM, IM, and PL bundles become twisted around each other until the attachment areas of the bundles form a triangular shape. The primary role of the ACL is to resist anterior tibial translation and internal tibial rotational loads of the knee joint. The ligament itself primarily consists of type I collagen oriented parallel to the longitudinal axis of the ligament providing it with tensile strength. The ACL receives innervation through nerve fibers from the posterior branches of the tibial nerve and has various mechanoreceptors to aid in knee joint proprioception including Ruffini receptors, Vater-Pacini receptors, golgi tendon organs, and free nerve endings functioning as nociceptors. These mechanoreceptors and nerve fibers provide afferent signaling for knee postural changes and influence motor activity in the muscles surrounding the knee. Loss of feedback from these mechanoreceptors, as in the case of an ACL injury, results an altered sense of joint position, quadriceps femoris weakness, and can affect maximal voluntary contraction of the muscle.

**PRIMARY ACL INJURY**

ACL injuries are the most common ligamentous injury in the knee, totaling between 100,000 and 200,00 injuries annually in the United States. These injuries most commonly occur in individuals under the age of 30, with some studies reporting ACL injuries accounting for up to 50% of all knee injuries in high school athletes.
incidence of these injuries has been slowly increasing in recent years, especially for females, likely due to increasing participation in high school and organized sports.\textsuperscript{17} There is also an increasing number of children participating in high-level athletics and older individuals who are remaining active longer, so the true incidence of ACL injuries and reconstructions is unknown.\textsuperscript{5} Contact mechanisms of injury appear to be more prevalent in high school-aged individuals (58.5\%),\textsuperscript{18} while non-contact mechanisms are more prevalent in individuals older than 18 years (67.2\% among men, 89.4\% among women).\textsuperscript{18,19} Mechanism of injury also differs by sex; in collegiate athletes, it was reported that 60\% of ACL injuries occurred by a non-contact mechanism for women versus 59\% occurring via a contact mechanism for men.\textsuperscript{20} Overall, men sustain more ACL tears compared to women\textsuperscript{21} due to a higher number of athletic exposures and greater participation in contact sports, but women have a higher rate of non-contact ACL tears after controlling for these exposures.\textsuperscript{18} Women have slightly higher ACL injury rates compared to men in sex-comparable sports at both the high school and collegiate levels.\textsuperscript{20,22} Among the general population, men have a higher incidence of ACL tears (241.0 per 100,000 person-years) between 19 and 25 years old and girls have a higher incidence (227.6 per 100,00 person-years) between 14 to 18 years old.\textsuperscript{21} In high school and collegiate level sports, the majority of ACL injuries occur during football and rugby in boys\textsuperscript{18,19} in comparison to soccer and basketball in girls.\textsuperscript{18} Women continue to sustain ACL injuries at higher rates than men comparably in collegiate soccer, basketball, and lacrosse.\textsuperscript{20}

Several other knee injuries may also occur concurrently with ACL tears.\textsuperscript{21,23,24} The term “unhappy triad” describes concomitant injuries to the ACL, meniscus, and
MCL at the time of injury. Prevalence of injury to the lateral meniscus and medial meniscus have been reported to be 54% and 51%,\textsuperscript{24} respectively, but may be as high as 60% in individuals with an ACL tear.\textsuperscript{21} MCL injuries are often under-reported, but may occur in 22% of individuals with ACL injuries.\textsuperscript{24} ACL injuries are also consistently associated with bone contusions of the tibial plateau and medial and lateral femoral condyles and are reported to occur in up to 84% of these individuals.\textsuperscript{23,24} The highest prevalence of bone contusions typically occur in the lateral femoral condyle and lateral aspect of the tibial plateau.\textsuperscript{24} It has been demonstrated that meniscal tears discovered during ACLR are not predictive of short-term poor clinical or radiographic outcomes; therefore, individuals with ACLR who sustained a concomitant meniscal injury will be included in our sample for this dissertation.\textsuperscript{25}

\textit{RISK FACTORS ASSOCIATED WITH ACL INJURY}

Many non-modifiable and modifiable risk factors for primary ACL injury have been identified. Non-modifiable risk factors of primary non-contact ACL injuries include female sex (specifically those without contraception in the pre-ovulatory phase), age (< 20 years), generalized ligamentous laxity, and narrow femoral intercondylar notch.\textsuperscript{26} Modifiable risk factors of primary ACL injuries include higher than normal BMI,\textsuperscript{27} dynamic valgus during sport specific movements, participation in sports requiring cutting and jumping movements, stiff landing mechanics at the hip and knee, poor lumbopelvic control, and weakness of hamstrings and hip abductors.\textsuperscript{26} Primary injury prevention programs that are appropriately implemented to focus on improving lower extremity strength, balance, agility, flexibility, and balance and incorporate plyometric exercise\textsuperscript{28}
may reduce the risk ACL injury by 50% in male and female youth athletes by targeting some of the aforementioned modifiable risk factors.

**ACLR EPIDEMIOLOGY**

Following an ACL injury, individuals may opt to remain ACL-deficient and seek conservative treatment through rehabilitation, while others pursue surgical intervention via reconstruction to regain knee joint stability. Approximately 130,000 ACL reconstructions (ACLRs) are performed annually in the United States, with the majority of these performed on individuals under the age of 20. From 2002 to 2014, the overall rate of ACL reconstruction increased by 22%, with the highest absolute rates of ACLRs increasing the most in individuals 13 to 17 years old. Among this age group, isolated ACLRs, ACLRs with meniscal repairs, and ACLRs with meniscectomies increased by 37%, 107%, and 63%, respectively. Since 1994, the number of ACLRs performed in the United States has increased in both male and female populations, with surgeries almost doubling among female patients. ACLR surgical costs were estimated to be nearly $1 billion in 2006 and have continued to rise. In 2019, a study using a large national database of over 14,000 patients determined the average cost for ACLR in the United States to be $24,707 ± 15,644.

**ACLR SURGERY**

Various techniques exist for ACLR including open versus arthroscopic surgery, intra- versus extra-articular, femoral tunnel placement, number of graft strands, graft bundle configuration, and graft fixation method. The important choice of which
technique and the type of graft that is used is typically dictated by the surgeon’s preference/training and the patient’s surgical history and opinion. Reconstructions with autograft (20-100% of ACLRs) and allograft (0-80% ACLRs) tissues are the most common. Autografts are tissues taken from one location on a patient’s body and transplanted to another location. The autograft tissue used in ACLRs usually consists of either the hamstrings (gracilllis and semitendinosus) tendons (HS) or bone-patellar tendon-bone (BPTB), but the quadriceps tendon (QT) can also be used. Allografts are tissue grafts taken from a human donor (cadaver). Common allograft tissues include: tibialis posterior tendon, Achilles tendon, tibialis anterior tendon, BPTB, and peroneus longus tendon.32 A recent study in 202133 reported that over the past 30 years ACLR graft choice among surgeons has evolved. Autograft tissues are preferentially utilized for primary ACLR over allograft and HS autografts have increased in popularity since the early 1990s.33 HS autografts now represent over 50% of ACLRs followed by BPTB at just under 40%, as compared to the most frequent graft choice being BPTB at nearly 90% in 1992. QT autografts have also increased in popularity since 2014, peaking at over 10% in 2018.33 Age largely dictates if individuals will be treated with autografts or allografts. Older individuals (>40 years) typically are treated with allografts, but those under the age of 29 are more often treated with autografts.34

Graft harvest location is also different based on region of the United States, with HS grafts most commonly used in the Midwest and West and BPTB grafts more likely in the Northeast and Southeast regions.34 One limitation in this data is that there were limited surgeons representing each of these regions so the differences may be
explained more by variations between surgeon graft choice preference rather than actual regional differences.  

Various systematic reviews comparing autografts versus allografts used for ACLR have determined that autografts offer greater patient satisfaction and improved outcomes when compared to allografts. ACLR with autografts is beneficial because it allows for earlier engraftment and no risk of rejection or disease transmission, but there is a potential for donor site morbidity. Allografts limit donor-site morbidity and thus typically have less post-operative pain and easier rehabilitation, but have possibility of disease transmission, slower incorporation of the new ligament (longer rehabilitation), and higher graft failures. A large retrospective cohort study of over 17,000 patients found that the overall ACLR revision (a reoperation to the knee where the original ACLR graft is replaced) rate was 2.45% (427/17,436) during 5 years of follow-up (mean 2.4±1.7 years) and allografts had a significantly higher revision rate of 2.81% as compared to HS autografts (2.37%) and BPTB autografts (1.94%). Autografts are preferred in young, active populations, but allografts can be a valid option in older, less active populations who are less likely to experience a re-injury. When comparing HS versus BPTB autograft, the majority of evidence suggests that there is no difference in clinical knee scores, laxity or rate of failure. However, some studies demonstrate that BPTB autograft is associated with lower retear risk compared with HS. BPTB autografts more frequently result in anterior knee pain and kneeling pain and there is a potential for persistent decreases in quadriceps (due to BPTB harvest) and hamstring (due to HS harvest) isokinetic muscle strength based on harvest location.
In addition to ACLR, patients often undergo other surgical procedures to fix additional tissue damage to the surrounding structures. Meniscectomies are the most common concomitant procedure and should be considered as an important risk factor for developing osteoarthritis (OA). Individuals undergoing ACLR and meniscectomy are 3.54 (95% CI = 2.56 - 4.91) times more likely to develop knee OA compared to individuals undergoing an isolated ACLR at 10.7 and 24.5 years post-surgery. This is also concerning because individuals with knee OA display reduced PA by on average 3,000 less steps per day compared to individuals without knee OA.

SECOND ACL INJURY

Although ACLR is typically successful in regaining knee joint stability following ACL injury, over 20% of individuals under the age of 25 will sustain a secondary ACL injury (including both ipsilateral graft tears and contralateral limb ACL tears) within just 15 years following ACLR. It has also been reported that 29.5% of young individuals who return to sport will suffer a second ACL injury within just 24 months of returning. Whereas only 15% of individuals sustain secondary ACL tears within the broader population of individuals ages 10 to 64 years old. Within two years of surgery, individuals with a history of ACLR have a six times greater risk of sustaining a second ACL injury to the involved or contralateral limb compared to those without a history of ACLR. In one population-based cohort study evaluating the incidence of second ACL injuries over a 10 year span, 13.8% of individuals were diagnosed with a secondary ACL tear and about 50% of these occurred in the contralateral knee. Approximately 75% of these secondary ACL injuries resulted from a non-contact mechanism. For
those who sustain a second ACLR, it means partaking in even more sedentary behavior associated with surgery and rehabilitation time. Therefore, individuals who have sustained multiple ACLRs may be at even greater risk of developing reduced PA engagement and characteristics associated with long-term cardiovascular health consequences.

**RISK FACTORS FOR A SECOND ACL INJURY**

Factors that have been associated with a higher risk of sustaining a second ACL injury on the ipsilateral limb resulting in revision ACLR include use of an allograft, HS autograft versus BPTB, male sex, younger age, and having a lower BMI. Younger age, female sex, and lower BMI are associated with having a higher risk of sustaining an ACL injury on the contralateral limb. The probability of sustaining a second ACL injury increases three to six times for athletes under the age of 20 years old. Additionally, women with a history of ACLR are two times more likely to sustain a contralateral ACL tear compared to an ipsilateral graft re-tear, whereas men with a history of ACLR have a 38% higher risk of re-tearing the graft on the ipsilateral side. A case control study in high school and college aged female athletes identified younger age, increased hip anteversion, decrease sport participation prior to first ACL injury, and decreased anterior stiffness of the contralateral knee (due to bracing) as risk factors for contralateral ACL tear. A multisite prospective cohort study reported that young, male patients with a hamstring autograft were at increased risk of sustained an involved limb ACLR revision, but young, females patients were at increased risk of sustaining contralateral limb ACL tears. Overall, patients with allografts tend to have a
significantly higher graft failure rate compared to patients with autograft (HS, BPTB) especially from the ages of 10 to 19 years.\textsuperscript{52} Time since surgery has also been shown to be associated with risk of sustaining a secondary ACL injury. Individuals with a primary ACLR who returned prior to 9 months post-surgery were 50\% more likely to sustain a secondary ACL tear compared to individuals returning after 9 months post-surgery.\textsuperscript{52} The factors above are important to consider when choosing reconstruction graft type and time of return to play after primary ACLR, particularly for young individuals interested in returning to PA and sport participation.

**EPIDEMIOLOGY OF CARDIOVASCULAR DISEASE (CVD)**

Cardiovascular disease (CVD) is the most common cause of mortality in high-income countries across the globe.\textsuperscript{53} Based on data from the National Health and Nutrition Examination Survey from 2015 to 2018, the prevalence of overall CVD including coronary heart disease (CHD), heart failure, stroke, and hypertension, in adults over 20 years of age in the United States is 49.2\% and increases with age in both males and females.\textsuperscript{54} CVD prevalence drops to 9.3\% in the population when hypertension is excluded.\textsuperscript{54} The Framingham Heart Study has been one of the largest and most important epidemiological studies evaluating predisposing factors for CVD and potential opportunities for prevention. It began on September 29\textsuperscript{th}, 1948 and has contributed to identification of physical inactivity, CRF, high blood pressure, high cholesterol, and obesity as risk factors for CVD morbidity and mortality.\textsuperscript{55} More recently, the American Heart Association in conjunction with the National Institutes of Health has reported on health behaviors and risk factors that contribute to overall cardiovascular
health. These include smoking, PA, diet, body weight, cholesterol, blood pressure, and glucose control.\textsuperscript{54} For the purpose of this dissertation we will focus on insufficient PA, obesity, and CRF.

CVD RISK FACTORS – INSUFFICIENT PHYSICAL ACTIVITY

The American Heart Association has identified meeting the United States Department of Health and Human Services (USDHHS) PA guidelines as one of their 7 components of ideal CV health for children and adults, as it is well known that physical inactivity is a major risk factor for both CVD and stroke.\textsuperscript{53} The various benefits associated with PA have been well-documented;\textsuperscript{56} such as improvements in mental health\textsuperscript{57} and risk factors for CVD (high blood pressure and cholesterol),\textsuperscript{53} and risk reduction for development of chronic, non-communicable diseases, yet many healthy young adults do not meet current PA recommendations.\textsuperscript{58} As of 2018, only 26\% of adult men, 19\% of adult women, and 20\% of adolescents reported sufficient activity to meet the current aerobic and muscle-strengthening guidelines.\textsuperscript{59} Physical inactivity is an independent risk factor for mortality and morbidity\textsuperscript{59} and it is estimated to cause 9\% of premature mortality. Additionally, it is responsible for disease burden of 6\% of CHD, 7\% of type 2 diabetes, 10\% of breast cancer, and 10\% of colon cancer.\textsuperscript{60}

Improving PA participation throughout an individual’s lifespan can have long lasting benefits. Lee et al. determined that elimination of physical inactivity would potentially increase world population life expectancy (0.68 years) similar to the well-established risk factors of obesity and smoking.\textsuperscript{60} The prevalence of physical inactivity (35\%) worldwide has now exceeded the prevalence of smoking (26\%).\textsuperscript{53} Therefore,
barriers to participation in appropriate amounts of MVPA, such as traumatic knee injuries, should be considered when evaluating risk factors for long-term CV health impairments.

**PHYSICAL ACTIVITY IN THE GENERAL POPULATION**

The 2018 Physical Activity Guidelines Advisory Committee released new recommendations stating that youth aged 6 to 17 should participate in 60 minutes of MVPA per day and adults should complete either 150 to 300 minutes of moderate intensity activity or 75 to 150 minutes of vigorous PA per week with two days of strength training.\(^9\) There is abundant evidence to suggest that PA is beneficial for improving and maintaining an individual’s physical and psychological health, yet less than 30% of the male population and less than 20% of the female population in the United States is currently meeting recommended guidelines for PA.\(^{61}\) Similar trends were noted in 2015 when prevalence of adults meeting the 2008 PA guidelines was assessed to determine differences based on age, sex, and race/ethnicity.\(^{62}\) Only 25.3% of males and 17.9% of females met PA guidelines for aerobic and strengthening activities. Race and ethnicity differences were also noted. The group with the highest percentage meeting guidelines was non-Hispanic white individuals at 23.4%, while only 16.8% of those who identified as Hispanic or Latino met PA guidelines.\(^{62}\)

Promotion of PA participation across the lifespan is imperative for promoting healthy lifestyles. Longitudinal studies suggest low to moderate evidence of PA behavior stability tracking from childhood and adolescence to adulthood, meaning that individuals that were more active in their childhood or adolescence remained more
This demonstrates the importance of promoting PA and sports participation during childhood and adolescence to increase PA engagement in adulthood and throughout the lifespan. This is especially important in individuals who have experienced a traumatic knee injury and subsequently developed OA. As mentioned previously, there is evidence to support a decline in PA later in the lifespan that occurs as a result of chronic joint diseases such as knee OA.

MEASURING PHYSICAL ACTIVITY

There are four dimensions of PA that are often referred to as the FITT principle when evaluating and characterizing PA engagement. The dimensions are frequency, intensity, time, and type of activity. Frequency indicates how often activity is performed (e.g. days per week), intensity describes the rate of energy expended during activity (e.g. absolute - metabolic equivalent of a task, relative – effort in relation to an individual’s aerobic capacity, percent of 1 repetition maximum for resistance activities), time quantifies the duration of activity that is performed, and type indicates the activity modality (e.g. running, cycling, swimming, weight training, etc.). PA volume describing the frequency and duration of activity (e.g. minutes per day/week) and can be used to quantify activity intensities such as MVPA. There are two main categories of methods used to assess PA: 1. Subjective methods using self-reported questionnaires/surveys or PA diaries/logs and 2) objective or device-measured methods that use wearable monitors such as pedometers, accelerometers, and consumer-grade smart watches or fitness trackers. Commonly utilized tools to assess self-reported PA in individuals with a history of ACLR include the Tegner Activity Scale, Marx Activity Scale (Marx Scale), and
the International Physical Activity Questionnaire Short Form (IPAQ-SF). Self-reported measures of PA provide more context regarding type of PA engagement that is not captured in more objective assessments and they are also more cost efficient. However, self-report measures can be prone to recall bias and their validity for capturing unstructured activities is questionable. Accelerometry has also been used in this population as an objective device-measured way to assess PA in free-living conditions. Objective monitoring provides information regarding frequency, intensity, and duration of PA, but does not provide information regarding type. Cost may also be a barrier for using use of PA tracking devices.

SELF-REPORTED PA – THE TEGNER ACTIVITY SCALE

The Tegner Activity Scale (Appendix A) consists of a single number item ranging on an 11-point Likert scale (0-10). This self-reported activity level scale was originally designed for administration by physicians to measure activity changes in the early stages following ACLR up to when an individual may be returning to work or later in the rehabilitation process when returning to recreational activities or sport. Reporting a score of 0 indicates the individual is unable to participate in activity due to knee disability, scores of 1-5 indicate increasing levels of participation in work or recreational sports, and scores 6-10 indicate increasing levels of recreational and competitive sport activity participation. The Tegner Activity Scale has been validated at 2, 6, 9, 12, and 24 months post-surgery in individuals with a history of ACLR. The Tegner Activity Scale demonstrated acceptable test-retest reliability (Intraclass Coefficient (ICC) = 0.82, 95% CI = 0.66 to 0.89) and a minimal detectable change of 1 on the Likert scale in this
Pre-operative data was used to establish criterion, content, and construct validity. The Tegner Activity Scale showed weak criterion validity compared to the Short Form-12 ($\rho=0.2, p<0.05$), acceptable construct validity on all six proposed constructs, and acceptable content validity with less than 30% of patients demonstrating floor (8% of participants reported the lowest score of 0) or ceiling effects (3% of participants reported the highest score of 10). Regarding survey responsiveness, the Tegner Activity Scale exhibited large effect sizes at all time points except at 6 months when the scale score showed moderate effect sizes. Although it does demonstrate acceptable reliability, validity, and responsiveness for measuring PA level in individuals with ACL injuries and history of ACLR; the Tegner Activity Scale is poorly correlated with MVPA assessed via accelerometry in both individuals with ($\rho=0.31$) and without ACLR ($\rho=0.07$). Additionally, it has been criticized for relating activity to specific sports rather than to functional activities that would be required for an individual to participate in the sports, potentially limiting its generalizability for use in all patients.

SELF-REPORTED PA – THE MARX ACTIVITY SCALE

The Marx Activity Level Scale (Marx Scale) (Appendix B) was created as a short, patient-reported activity assessment for reporting a patient's highest peak activity over the past year. It consists of four items to assess running, cutting, pivoting, and decelerating. Each item is scored from 0 to 4, based on the frequency it is performed from less than once per month (0 points) to four or more times per week (4 points), with a minimum of 0 to a maximum of 16 points possible. The strength of using this scale is that it focuses on evaluating components of physical function that are common in sports
rather than an individual's participation in specific sporting activities. The Marx Scale has been shown to have both face and content validity as determined by physicians and health care professionals in a rehabilitation setting. Additionally, construct validity has been determined via relationships with other self-reported activity scales. The Marx Scale was significantly correlated with all of the activity rating scales that it was compared to including a moderate relationship with the Tegner Activity Scale ($r = 0.66$, $p<0.05$), but had a poor relationship ($p = 0.15$) with MVPA assessed via accelerometry. Divergent validity was established based on an inverse relationship between the Marx scale ($r = -0.48, p = 0.002$) and age according to the hypothesis that individuals will become less active as they age. The Marx Scale demonstrated excellent test-retest reliability at 1 week (ICC = 0.97).

For individuals with knee injuries and pathologies, the Marx scale has been shown to be valid and reliable for measuring type and volume of activity.

SELF-REPORTED PA – THE IPAQ-SF

The International Physical Activity Questionnaire – Short Form (IPAQ-SF) (Appendix C) is a 9-item self-reported questionnaire assessing time spent in sitting, walking, moderate, and vigorous activities over the course of 7 days. This questionnaire is one of the most widely used assessments of subjective PA globally, especially in epidemiological and longitudinal studies of PA. In adults, the IPAQ demonstrates good test-retest reliability with an overall ICC of 0.86 (walking ICC = 0.89, moderate activity ICC = 0.71, vigorous activity ICC = 0.86). In adolescents ages 13 to 18, test-retest reliability ranged from poor to moderate and therefore should be used.
with caution in this population. The IPAQ has been validated against various PA measures including accelerometers and fitness measures (e.g., VO$_2$max, treadmill time). The IPAQ-SF demonstrated negligible to small relationships with objective measurement devices when assessing total PA and showed moderate relationships when assessing walking. It also showed small correlations (range $\rho = 0.16$ to 0.36) with fitness measures. According to the available evidence, the use of the IPAQ-SF as a measure of PA is fairly weak, although it is widely used. Overall, it should be noted that the IPAQ-SF tends to overestimate PA volume when compared to device-based PA monitoring.

DEVICE-MEASURED PA – ACCELEROMETRY

Device-measured monitoring using PA monitors was introduced in the 1980s and over the past few decades accelerometer-based PA monitoring has become a prominent way to assess free-living PA. The strength of accelerometry lies in its ability to effectively measure activity in free-living conditions to overcome the barriers of bias in self-report and other subjective measures. Many research- and consumer-grade activity monitors exist, but this literature review will focus on the ActiGraph GT9X Link, the most recent generation of ActiGraph’s accelerometers due to its use for objectively measuring PA in the proposed study methodology. The GT9X Link monitor is a triaxial capacitive accelerometer that also contains a triaxial magnetometer and gyroscope. The GT9X Link monitor determines number of counts per minute based on Actigraph’s proprietary algorithm that accounts for changes in acceleration along three different axes. Newer ActiGraph monitors are now able to assess activity data based on vector
magnitude (VM), which is the square root of the sum of squares of data from each of the three axes (X, Y, Z) (Equation 1).72

\[ VM = \sqrt{X^2 + Y^2 + Z^2} \]

Activity counts consider intensity of an individual’s movement, with more intense movements (e.g. running) being represented by more activity counts per minute when compared to less intense activities (e.g. walking). Selection of appropriate data collection protocols and data processing criteria are essential to establish before data collection is initiated. It is recommended that accelerometers are worn on the waist (over the anterior superior iliac spine) using sampling frequencies of 30, 60 or 90 Hz with a normal filter using an epoch length of 60 seconds for adults and 15 seconds or less for children and adolescents.71 They are typically distributed for a 7 day wear period and valid data requires wear time for at least 10 hours per day for at least 4 days (including 1 weekend day).71–73 The ability to assess different activity intensities and step counts is done via cut-point metrics based on counts per minute (cpm). The Freedson 1998,74 Freedson 2011 VM,75 and Troiano 200876 are some of the most commonly used cut-point measurements for adults. Freedson 1998 cut-points use counts from the vertical axis (Y or VA) to determine sedentary (0-100 cpm), light (101-1951 cpm), moderate (1952-5724 cpm), and vigorous (<5724 cpm) PA intensities.74 The Freedson 2011 VM cut-points use VM data counts to determine sedentary (0-200 cpm), light (201-2690 cpm), moderate (2691-6166 cpm), and vigorous (>6166 cpm) PA intensities.75 The Troiano cut-points were developed in 2008 and have been used to establish the prevalence of US adults meeting current PA guidelines. They utilize VA counts to determine sedentary (0-100 cpm), light (100-2019), moderate (2020-5998),
and vigorous (≥5999 cpm). For children and adolescents, the Evenson cut-points use counts from the VA to determine sedentary (0-100 cpm), light (101-2295), moderate (2296-4011), and vigorous (≥4012). Total volume of PA can also be assessed using total activity counts (TACs) which can be calculated based on total VM counts or counts from axis 1 (VA). In order to determine PA time at varying intensities (i.e., sedentary, light, moderate, vigorous), Freedson 1998, Freedson 2011 VM, Troiano 2008, or Evenson 2008 cut points are commonly used, while TACs are typically utilized to measure total PA during the wear-period. In all analyses it is important that the researcher controls for monitor wear time to account for differences in PA based on how often the monitor was worn.

Reliability and validity have been determined for the different generations of ActiGraph models over the years using various methods, but limited data is available for the ActiGraph Link monitors. In a recent study by Montoye et al., both raw data and counts were compared between the ActiGraph Link and ActiGraph GT3X+ with the finding that count data were more comparable than the raw data between accelerometers. The two accelerometers also showed similar estimates regarding activity intensity with the count data when using the Freedson 1998 and Freedson 2011 VM equations. Taken together, this means that the two monitors can be used interchangeably when collecting count data, which is important for making comparisons between studies using the monitors. However, researchers should be aware that there are some potential differences with raw activity data.

In adults, one week of accelerometer data has been shown to be representative of habitual PA. It is recommended that adults wear activity monitors for at least 4 days
to achieve 80% reliability when assessing TACs or MVPA and at least 7 days of monitoring are required to obtain reliable measures of physical inactivity.\textsuperscript{79} When worn for 4 days for at least 10 hours per day, the monitors demonstrate good test-retest reliability over two 7-day periods separated by 1 to 4 weeks (ICC = 0.77 to 0.90).\textsuperscript{78} During lab based treadmill walking, ActiGraph monitors were correlated to manual step counting (ICC = 0.72, p<0.001) and tended to underestimate step counts at lower speeds (2.4-3.2 km/h) when compared to manual step counts.\textsuperscript{80} These monitors also showed a sensitivity of 83% and specificity of 89.6% when identifying MVPA compared to indirect calorimetry during a submaximal walking test.\textsuperscript{80}

Doubly labeled water (DLW) can be used to validate energy expenditure during PA as it can be used in free-living conditions over several days. DLW requires urine, saliva or blood specimens and is assessed using mass spectroscopic analysis to detect elimination rates of oxygen-18 and deuterium.\textsuperscript{81} DLW has been shown to have weak to moderate correlations with ActiGraph TACs, steps, and accelerometer-estimated energy expenditure (TACs \(\rho = 0.33-0.44\), Steps \(\rho = 0.42\), \(\rho = 0.39-0.44\)).\textsuperscript{81} Overall, device validity has been shown to vary based on the activity and validation test to which the monitor is being compared.

**PHYSICAL ACTIVITY AFTER ACLR**

Return to sport following ACLR is the desired outcome for 84% individuals who were active prior to injury;\textsuperscript{82} however, not all individuals return to sport participation post-surgery. Approximately 81% of individuals return to any level of sport, 65% of individuals return to pre-injury level of sport, and only 55% of individuals return to
competitive levels of sport within 2 years of surgery. However, until recently, it was unclear if individuals maintained adequate PA participation regardless of their return to sport status. These reductions in sport-based PA following surgery highlight the importance of measuring PA in individuals with ACLR. The most common methods of assessing PA in those with a history of ACLR are the Tegner Activity Scale, the Marx Scale, the IPAQ, and accelerometry.

When comparing young individuals within five years of ACLR and healthy controls, no differences in median Tegner Activity Scale scores (ACLR: 6 [interquartile range (IQR), 5-8]; control: 7 [IQR, 6-8]; \( p = 0.12 \)) or median Marx scores (ACLR: 11 [IQR 7-14]; control: 12 [IQR, 8-13]; \( p = 0.85 \)) were reported between groups.\(^1\) Individuals with ACLR who were further out from surgery (average 20 years, range 17-28 years) have reported decreased Tegner Activity Scale scores compared to healthy, age- and gender-matched controls (ACLR = 4; control = 6, \( p = 0.001 \)), but reported no differences in IPAQ scores (ACLR = 1563; control = 1893, \( p = \text{NS} \)).\(^8\) Additionally, only weak correlations were observed between step count and Tegner Activity Scale score (\( r = 0.36, p = 0.04 \)), while no relationships between step count and the Marx score (\( r = 0.16, p = 0.27 \)) were shown.\(^8\) It has been previously shown that correlations between the Tegner Activity Scale, Marx scale, and objectively measured PA are weak and non-significant in patients with ACLR,\(^8\) indicating a disconnect between self-reported PA and actual objective PA participation.

Overall, individuals with ACLR engage in reduced participation in device-measured PA compared to individuals without a history of lower extremity injury, but no differences exist in self-reported PA. Adult individuals with ACLR participated in lower
step counts (ACLR = 8158 ± 2780 steps/day; control = 9769 ± 2785 steps/day) and less MVPA time (ACLR = 79.37 ± 23.95 min/day; control = 93.12 ± 23.94 min/day) compared to age- and sex-matched healthy controls.\(^1\) Individuals with a history of ACLR were also 2.36x (95%CI = 1.09 - 5.08) less likely to meet USDHHS PA guidelines of 150 minutes of aerobic PA per week compared to healthy individuals.\(^3\) Another common PA recommendation is taking 10,000 steps per day;\(^58\) however, only 24% of individuals with ACLR met this guideline compared to 42% of healthy controls in the study.\(^3\) Overall, individuals with ACLR in this study participated in less MVPA (by about 15 minutes) and 1,600 less steps per day compared to healthy controls.\(^1\) Among adolescents, there are mixed findings regarding PA participation following knee injury. No differences in MVPA were observed when comparing adolescent female athletes within 1-2 years of ACLR to uninjured athletes, but female athletes with ACLR did participate in fewer mean minutes per day of vigorous PA.\(^9\)

More recent evidence is indicating that individuals with ACLR have reduced PA participation. Because of the well-established role of sedentary behavior in the development of chronic disease and premature mortality, it is concerning that individuals with a history of ACLR are participating in less PA compared to the general population without knee injuries. It is even more concerning that these individuals are typically young and highly active prior to injury, so it is possible that ACLR may be a catalyst for development of negative long-term CV health outcomes.
CVD RISK FACTORS – OBESITY

Overweight and obesity are major risk factors associated with CVD, specifically relating to CHD, stroke, atrial fibrillation, and congestive heart failure (CHF) and have been identified as another one of the seven components of ideal CV health. According to National Health and Nutrition Examination Survey (NHANES) from the years 2013-2014, the age-adjusted prevalence of obesity was 37.7% among adults ages 20 and older. Even more concerning is the prevalence of overweight (16.2%) and obesity (17.2%) in children ages 2-19 during this time. More recently, the National Center for Health Statistics reported that based on 2017-2018 data that 16.1% of children ages 2-19 were considered overweight and 19.3% were considered obese, with more specifically 21.2% of adolescents aged 12 to 19 years old being considered obese. In 2017-2018, it was estimated that 30.7% of adults over the age of 20 were considered overweight and 42.4% of adults were considered obese. This information can be used to infer that prevalence of obesity in the US is rising among adolescents and adults and many individuals who are experiencing ACLR may also be overweight or obese.

According to the National Longitudinal Study of Adolescent Health, adolescents who were obese had a 16 times greater risk of having severe obesity as adults. Additionally, in this sample 70% of adolescents with severe obesity maintained this weight status into adulthood, highlighting the ability of weight status to track throughout the lifespan. Participation in PA is one way to help individuals, both children and adults, maintain body weight over time and can also reduce the risk of weight gain and incidence of obesity across the lifespan. Reduced PA engagement among young individuals with ACLR may have a negative impact on weight status that could have
long-standing consequences for future CV health. BMI is a simple, commonly used tool to assess body size as it relates to obesity and disease risk in both healthy and ACLR populations. Currently, there is limited information available characterizing body composition profiles of individuals with ACLR.

**MEASURES OF BODY SIZE AND BODY COMPOSITION**

BMI is an important health-related outcome used as a measurement of body size which considers an individual’s height and weight using the equation (Equation 2):^62

\[
\text{Equation 2: BMI} = \frac{\text{body mass (kg)}}{\text{height (meters)}^2}
\]

The same equation is used for children and adolescents, but BMI percentiles are also calculated, and values are compared to national percentiles based on age and sex. In the adult population, the following cut-points are used for BMI: underweight - less than 18.5 kg/m\(^2\), normal/healthy weight - 18.5 to 24.9 kg/m\(^2\), overweight - 25.0 to 29.9 kg/m\(^2\), and obese - greater than 30.0 kg/m\(^2\). BMI percentiles are utilized for children and adolescents: underweight - less than the 5\(^{th}\) percentile, normal/healthy weight - 5\(^{th}\) to 85\(^{th}\) percentile, overweight - 85\(^{th}\) to 95\(^{th}\) percentile, and obese - greater than the 95\(^{th}\) percentile.

BMI has been investigated thoroughly as a proxy measure of adiposity and all-cause mortality. Greater BMI is positively associated with various noncommunicable diseases including diabetes, high blood pressure, high non-HDL cholesterol, stroke, and ischemic heart disease.^90 While BMI is a simple calculation and clinically applicable quantification of body size in large sample sizes, it is a limited measure because it fails to differentiate between fat mass and fat-free mass. Depending on an individual’s
height, individuals with high lean mass may be classified as overweight or obese, but have low or normal fat mass. This is an important limitation of BMI to acknowledge because of the negative associations that exist between high fat mass and poor health outcomes.

**BMI AND ACLR**

Overall, BMI has not been adequately tracked longitudinally following ACLR making it difficult to establish the relationship between ACLR and greater BMI following surgery. Adults with a history of ACLR typically have higher BMIs compared to pediatric patients (adult = 27.2±0.7 kg/m², pediatric = 24.3±1.1 kg/m², p<0.01). This trend was similar in both male and female patients. Another study tracked BMI at one, three, and six months post-ACLR, but separated individuals into low and high BMI groups prior to analyses. No significant differences in BMI were reported between time points in the low or high BMI group after ACLR, indicating that average BMI in the low and high groups were relatively unchanged across time points. This study failed to consider potential individual changes in BMI and whether certain groups of individuals are more likely to demonstrate BMI changes following ACLR.

Recently, a study in pediatric patients with ACLR identified a significant unfavorable change in BMI percentile following surgery. Patients in the normal-weight category gained on average more than 4 BMI percentile points in the 2 years following ACLR (peaking at 9 months post-ACLR). Similarly, another study observed elevated BMI for adolescent female athletes in the first year following a knee injury. In those who reported a knee injury, they experienced significantly greater increases in BMI.
percentile (by up to 5 points more) relative to their uninjured peers. Lastly, on average 20 years after ACLR, it was reported that individuals had higher a BMI compared to healthy, gender- and age-matched controls. It is possible that those who had an ACL injury had a higher BMI at the time of injury, but this evidence may also indicate that there are persistent weight changes long-term in the months and years following ACLR. Due to the relationship between higher BMI and CVD morbidity and mortality risk, BMI is important to assess in this population. It is interesting to note that although BMI may have poor long-term effects on health, it has been shown that individuals with a higher BMI had a lower risk of revision ACLR. Individuals in the overweight category (BMI 25-29 kg/m²) had a 30% lower risk (95% CI [12-44%]) and those in the obese category (BMI 30 kg/m²) had a 33% lower risk (95% CI [12-49%]) when compared with those in the normal category (BMI <25kg/m²). Similar relationships were present for risk of sustaining a contralateral injury. This data indicates that a higher BMI may help to reduce risk of requiring a revision ACLR on the ipsilateral limb in the years following surgery. This information also presents the possibility that this reduced risk may be due to less participation in PA or activity exposures that place an individual at risk of a reinjury and thus the potential for weight gain and a higher BMI. However, there is other information to suggest that elevated BMI that is greater than 25.0 kg/m² is a risk factor for early ACL revision. There is also evidence to show that patients with elevated BMI are more likely to have longer surgical times and require additional surgery at the time of ACLR. Lastly, BMI is also a strong predictor of both development and progression of OA. The risk of OA increases by 35% (95% CI [1.18-1.53], p<0.001) with a 5.0 kg/m² increase in BMI. Overweight status is associated with a 2.45 times higher risk of knee
OA (95% CI [1.88-3.20], p<0.001) and obesity is associated with a 4.55 times higher knee OA risk (95% CI [2.90-7.13], p<0.001).97 Taken together, there is a need for further study of longitudinal changes in BMI and how it is related to health status in individuals with a history of ACLR.

**BODY COMPOSITION – AIR DISPLACEMENT PLEHTYSMOGRAPHY**

Body composition is the proportion of fat mass and fat free mass in the body. Body composition can be assessed using numerous techniques including hydrodensitometry (underwater weighing), bioelectrical impedance analysis (BIA), skinfold calipers, dual-energy x-ray absorptiometry (DXA), and via air displacement plethysmography (BodPod). Air-displacement plethysmography has several advantages over other validated measurement techniques, including a quick, non-invasive, and safe measurement process that allows for the accommodation of various subject types (e.g. children, obese, elderly, and individuals with a disability).98 Full procedures for the BodPod assessment can be found elsewhere,98 but will be described here briefly. Air-displacement plethysmography allows for the volume of the human body to be measured indirectly by measuring the volume of air that it displaces inside of the closed chamber. The air inside the chamber can be measured by applying Boyle’s gas law, which states that at a constant temperature, pressure (P) and volume (V) are inversely related (Equation 3).

\[ P_1V_1 = P_2V_2 \]
The participant is also weighed with an electronic scale to obtain body mass for use in the calculation of body density. Body density is calculated using Equation 4.

\[
\text{Equation 4: Body Density} = \frac{\text{Body Mass}}{\text{Body Volume}}
\]

Body density is then converted to percent body fat using a standard formula such as the modified Siri equation.\textsuperscript{99} Previous research has shown that the BodPod provides a reliable and valid estimation of body fatness in the general population.\textsuperscript{100}

**BODY COMPOSITION FOLLOWING ACLR**

Currently, there are a limited number of studies with assessments of body composition in individuals with ACLR. One study evaluated peripheral soft tissue composition via MRI and its relationship with outcomes following ACLR. They found that periarticular fatty-connective tissue was trending toward predicting negative outcomes in individuals with ACLR.\textsuperscript{101} In another study, young female athletes who reported a knee injury experienced an increase in body fat percentage by up to 1.5% as compared to their uninjured peers.\textsuperscript{94} Triplett and Kuenze\textsuperscript{2} reported that women with a history of ACLR (within 5 years post-surgery) had higher percent body fat (32.7±6.7.% versus 22.6±4.9%; p<0.01) than uninjured age- and activity level-matched women. Limited conclusions can be made based on the small sample size of this investigation (N=20) and the inclusion of only female participants.\textsuperscript{2} Due to the limitations associated with BMI and the lack of information available regarding body composition in this population, a clearer picture of the influence of fat mass on CV health outcomes should be established with the measurement of body composition in individuals with ACLR.
CVD RISK FACTORS – CARDIORESPIRATORY FITNESS

There is mounting evidence establishing that low levels of CRF are associated with a high risk of CVD, all-cause mortality, and mortality attributable to various cancers. Both clinical and epidemiological evidence has demonstrated that CRF may be a stronger independent predictor of mortality than already well-established traditional risk factors such as hypertension, high cholesterol, smoking, and type 2 diabetes. Reclassification of risk for adverse outcomes also improves when CRF is included in addition to traditional risk factors. Although there seems to be a dose-response relationship between CRF and health outcomes, attainment of extremely high CRF levels is not necessary to provide significant health benefits. It has consistently been shown that the greatest benefits for health occur when an individual progresses from the least fit group to the next least fit group. The apparent negative effects of ACLR on PA participation are especially concerning given that consistent participation in PA is the strongest predictor of CRF. However, the addition of small increases in PA may also translate to improvements in CRF and large overall health benefits.

MEASURING CARDIORESPIRATORY FITNESS

CRF is a measure of the body’s integrated ability to transport oxygen from the atmosphere to the mitochondria and utilize it to perform physical work. Functional capacity is dependent on a series of processes including the pulmonary ventilation and perfusion, appropriate function of the atria and ventricles in the heart, efficient transport of blood via the vasculature from the heart to the working muscle cells, and the capacity
of working muscles to utilize oxygen. CRF requires the integrated function of many body systems and thus provides an adequate representation of overall health.

GRADED EXERCISE TESTING

The gold standard for assessing CRF is measuring maximal oxygen consumption (VO$_{2\text{max}}$) during a graded exercise test such as the Bruce Protocol. CRF can also be estimated using the peak work rate achieved or a submaximal exercise protocol on a cycle ergometer or treadmill. There are also non-exercise algorithms available. Although measurement of VO$_{2\text{max}}$ is more valid and objective, estimated CRF calculated from peak work rate is often utilized in large epidemiological studies due to convenience. Both measured and estimated CRF strongly predict health outcomes. An extensive body of evidence has established that individuals with low CRF (aerobic fitness) have a higher risk of CVD, all-cause mortality, and mortality attributable to various cancers.

The apparent negative effects of ACLR on PA participation are especially concerning given that consistent participation in PA is the strongest predictor of CRF.

Limited information is available regarding CRF profiles following ACLR in young adults who are not classified as elite athletes. Almeida et al. reported that CRF was significantly reduced in professional soccer players with ACLR and aerobic function was not restored after 6 months of structured rehabilitation when compared to non-injured athletes of the same competitive level. It is possible that 6 months was not enough time following surgery for these athletes to adequately return to training in order to regain aerobic fitness. However, it is challenging to generalize these findings based on the baseline CRF levels among elite soccer athletes. Another study investigated the
cardiac effects including CRF of a period of deconditioning (mean time of reduced PA = 2 months) followed by reconditioning in a group of athletes with an ACL injury.\textsuperscript{105} All athletes in the study underwent a maximal exercise test via cycle ergometer when the treating clinician determined that the injured knee was stable enough for the test and it was repeated again 6 months later following a phase of reconditioning. Absolute VO$_{2\text{peak}}$ increased significantly ($p<0.001$) during the reconditioning phase by over 7\% from 3454 ± 557 ml/min to 3671 ± 571 ml/min.\textsuperscript{105} Olivier et al. also evaluated physiological adaptations to deconditioning and reconditioning using a single leg cycling training program following ACLR in amateur soccer athletes.\textsuperscript{106,107} Athletes in the cardiorespiratory training group maintained their VO$_{2\text{peak}}$ after 6 weeks of rehabilitation as compared to the control group who participated in rehabilitation without the aerobic training program. The control group experienced a significant decrease in VO$_{2\text{peak}}$ by 10\% (as determined by a single-leg cycle ergometer maximal exercise test). In this study, the athletes had been inactive for 2 months preceding surgery so it is possible that the decline in VO$_{2\text{peak}}$ may have already occurred prior to the training program.\textsuperscript{106} Unfortunately, in these studies VO$_{2\text{peak}}$ was not measured prior to or near the time of injury, so it is difficult to comment on how CRF may have changed from pre- to post-ACLR.

In the only study to our knowledge to investigate these variables among non-elite athletes, absolute VO$_{2\text{peak}}$ during a cycle graded exercise test was similar among a small sample of women with ACLR when compared to age- and activity-level matched controls (Table 1). However, when accounting for body mass, differences were seen in relative VO$_{2\text{peak}}$ with individuals with ACLR having significantly lower CRF than matched
healthy women. This difference in relative CRF was most likely due to significantly higher % body fat and fat mass in the women with ACLR rather than a true difference in CRF.²

Table 1. Cycle aerobic fitness and body composition results.²

<table>
<thead>
<tr>
<th></th>
<th>ACLR</th>
<th>Healthy</th>
<th>p-value</th>
<th>η_p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Fat (%)</td>
<td>32.7 ± 6.7</td>
<td>22.6 ± 4.9</td>
<td>&lt;0.01*</td>
<td>0.45</td>
</tr>
<tr>
<td>Fat Mass (kg)</td>
<td>25.4 ± 9.0</td>
<td>13.7 ± 4.1</td>
<td>&lt;0.01*</td>
<td>0.43</td>
</tr>
<tr>
<td>Fat Free Mass (kg)</td>
<td>50.1 ± 4.5</td>
<td>46.2 ± 4.9</td>
<td>0.05</td>
<td>0.17</td>
</tr>
<tr>
<td>Time to Exhaustion (min)</td>
<td>13.3 ± 1.8</td>
<td>13.2 ± 2.5</td>
<td>0.97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO_2peak (L*min⁻¹)</td>
<td>2.5 ± 0.3</td>
<td>2.4 ± 0.3</td>
<td>0.58</td>
<td>0.03</td>
</tr>
<tr>
<td>VO_2peak (ml<em>kg⁻¹</em>min⁻¹)</td>
<td>33.0 ± 5.7</td>
<td>39.5 ± 4.0</td>
<td>0.04*</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*P<0.05

An ACL tear has also been shown to be associated with negative alterations to the quadriceps muscle that impede the muscle's ability to generate and maintain strength.¹⁰⁸ Additionally, both detraining¹⁰⁹ and ACLR¹¹⁰ have been shown induce a shift of IIa fibers (fast-oxidative, fatigue-resistant) to type IIb fibers (fast-glycolytic, fatigable) and a reduction in fiber cross-sectional area.¹⁰⁹,¹¹⁰ This reduction in muscle size and loss of the typical aerobically focused metabolic characteristics suggests that when performing high intensity exercise, for example in the case of a graded exercise test, these type IIb fibers are subjected to greater metabolic strain compared to the typical size and abundance of IIa fibers in the healthy limb.¹¹¹ These features of the detrained muscle following ACLR may lead to an altered metabolic profile when evaluating CRF in these individuals with ACLR compared to healthy individuals. Taken together, the work examining CRF of individuals with ACLR indicates a reduction in CRF following surgery...
most likely due to a deconditioning period consisting of low intensity activity. It seems that patients may benefit from aerobic training during rehabilitation to help limit deconditioning during this time and encourage appropriate levels of PA as the patient transitions out of rehabilitation.

LACTATE METABOLISM AND THRESHOLD

Lactate plays a key role in the coordination of total-body metabolism. Normal serum lactate (L+ enantiomer) concentration is near 1.0 mM/L of blood at rest and can exceed 15 mM/L after a maximal exercise bout.\textsuperscript{112} Lactate is an energy intermediate that can be created in tissues undergoing high rates of glycolysis. It is distributed throughout the body in the blood and can be utilized as a precursor for glycogenesis and gluconeogenesis in addition to acting as a substrate for oxidizing tissues. Direct assessment of blood lactate response to exercise can be achieved via a fingerstick to obtain a blood sample. During incremental exercise that is progressive in nature, blood lactate will rise gradually from resting levels and then more rapidly with increasing exercise intensity. Lactate threshold (LT), onset of blood lactate accumulation (OBLA), and lactate maximum can be used to represent the blood lactate profile.\textsuperscript{113} LT is defined as the point when lactate production exceeds lactate clearance, while lactate maximum is the highest lactate measured during the course of an exercise test. OBLA is associated with reaching a blood lactate equivalent to 4.0 mM/L.

As mentioned previously, there may be an altered metabolic profile in individuals with ACLR driven by reductions in PA and fitness following surgery. Currently, there is limited evidence evaluating production of metabolic by-products in the ACLR population.
Patras et al. found only moderate relationships between markers of endurance (LT, OBLA) during high intensity running and EMG activity in the ACLR limb, compared to strong relationships in the healthy limb of individuals with ACLR. This finding provides evidence supporting the idea that there is a higher accumulation of metabolic by-products in the ACLR limb leading to a suppression in EMG signal, compared to the healthy limb. Chronic disturbances in the ACLR limb may modify the ability of the local muscle environment to tolerate PA at high intensities such as what would be needed during a graded exercise test.

MEASURES OF CARDIOVASCULAR HEALTH

BLOOD PRESSURE DURING EXERCISE

In healthy individuals, systolic blood pressure (SBP) increases linearly with increasing exercise intensity mainly due to increased cardiac output which enables an individual to meet the demands of exercising muscle. However, diastolic blood pressure (DBP) stays relatively static due to an overall reduction in total peripheral vascular resistance resulting from arterial vasodilation in the exercising muscle. There is no widely accepted normal blood pressure (BP) response to exercise, but abnormal exercise BP can manifest as either exercise hypotension (low BP response) or as an exaggerated exercise BP (high BP response). A drop in SBP below resting level and an initial increase during early exercise followed by a decrease by ≥10 mmHg are two common definitions of exercise-induced hypotension that serve as possible indications to terminate an exercise test due to them being consistently shown as a marker of increased risk for adverse events. An exaggerated BP response has been defined as
a maximal BP value of ≥210 mmHg for men and ≥190 mmHg for women. The American College of Sports Medicine (ACSM) also defines a BP response during an acute exercise bout of SBP >250 mmHg or DBP >115 mmHg as a relative indication for exercise test termination. Exaggerated BP response is considered an indicator of CVD risk, left ventricular hypertrophy, and CV events. There is also evidence to support a link between exaggerated exercise BP responses and latent hypertension risk. Factors such as age, sex, ethnicity, obesity, fitness level, and co-morbidities may have a significant influence on BP responses during graded exercise. One hypothesis relating CRF and BP is that CRF (and effort level during the test) could be acting as a factor influencing BP where individuals with a higher VO$_{2\text{max}}$ yield higher cardiac outputs during maximal exercise and thus have a greater peak SBP. Monitoring modulation of an individual’s BP response and maximal SBP during a graded exercise test can provide important information about CVD risk that is not described with an assessment of oxygen consumption and lactate response alone. Moreover, BP measurements during graded exercise testing have the potential to serve as an additional assessment of hypertension and CVD risk and diagnosis, which could be important in populations such as individuals with ACLR; particularly considering we have observed higher BMIs and reduced PA in individuals with ACLR. Lastly, higher exercise SBP responses have been positively correlated with increased arterial stiffness as measured by carotid-to-femoral pulse wave velocity.
CAROTID-TO-FEMORAL PULSE WAVE VELOCITY

Carotid-to-femoral pulse wave velocity (cfPWV) has been used to measure arterial stiffness, or the elasticity of the arterial wall, which has been recognized as an independent marker of CVD risk. Increased arterial stiffness is linked to an increased risk of CVD and mortality. Normal reference values collected from a population of 1455 subjects have been proposed, with individuals under the age of 30 displaying a mean (2±SD) cfPWV of 6.2 (4.7-7.6) m/s. The standard cut off-value for cfPWV in the prediction of CV events is 10 m/s. We do not expect to see cfPWV values >10 m/s of the participants we will be measuring in this dissertation because they will be ages 18-30, but increased cfPWV in patients with ACLR as compared to uninjured controls may be worth considering and provide preliminary evidence of CVD risk later in life.

cfPWV is defined as the speed of travel of the pulse between the carotid and femoral arterial sites and is calculated using the equation cfPWV = (0.8 × distance) ÷ Δt. Following the cfPWV assessment, distance between the common carotid artery and common femoral artery measurement sites is measured using a measuring tape and 80% of this distance is used because it is the most similar to the distance observed via MRI of the arterial tree. The pulse transit time (Δt) is the difference between the carotid pulse transit time and the femoral pulse transit time; this is calculated as the time delay between the R-spike of the ECG signal and the arrival of the arterial pressure waveform at each arterial site. To determine the arrival of the waveform at each site, arterial pressure waveforms are band-pass filtered (2-30 Hz) and the minimum value of the filtered signal is identified as the arrival of the waveform. A cfPWV can be calculated using 10 s data sections and the reported value is the average of two, 10 s
sections. If the difference between these two values is >0.5 m/s, a third 10 s data section is analyzed and the median of the three values is reported.\textsuperscript{124}

\textit{RELATIONSHIPS BETWEEN ARTERIAL STIFFNESS AND PA}

The amount of time spent in both light and moderate PA is associated with lower arterial stiffness, while sedentary behavior is associated with higher arterial stiffness.\textsuperscript{127,128} Arterial stiffening increases peripheral wave reflection, leading to an increase in ventricular afterload, a reduction in coronary perfusion, and myocardial hypertrophy and ischemia.\textsuperscript{129,130} While most research in this area is among older individuals, we hypothesize that it is possible that young people who exhibit sedentary behavior, such as those who are rehabilitating an injury may also develop increased arterial stiffness. Lower cfPWV has been observed in elderly individuals who walked 10,000 steps per day compared to walking 6,000 steps per day.\textsuperscript{131} There is evidence that changes in arterial stiffness can occur following only 6 days of intense endurance exercise in young men, however, this may be due to autonomic changes rather than structural changes in the vasculature.\textsuperscript{132} Physical deconditioning due to reduced PA is associated with enhanced vasoconstrictor tone and has effects on arterial remodeling, which most likely affects CVD risk.\textsuperscript{133} Immobilization of a limb due to trauma can also elicit changes to the vasculature due to inactivity, some of which could also be impacted by tissue healing and inflammatory processes.\textsuperscript{134} Studies of exercise training have also shown that structural and functional vascular adaptations can occur following training. The magnitude of such changes depend on training intensity and duration.\textsuperscript{133} Therefore, it is important to consider aerobic exercise training as potential intervention in individuals.
who have experienced periods of reduced PA with an injury such as those ACLR, as it could result in aberrant changes to the vascular structure and function. Because individuals with ACLR have been identified as a group displaying reduced engagement in PA, this information may have clinically relevant implications for incorporating more PA into the daily lifestyle and promoting exercise interventions in this population to reduce the risk of cardiovascular disease and all-cause mortality.

EVIDENCE FOR CARDIOVASCULAR IMPAIRMENTS FOLLOWING ACLR

Currently there is limited information available regarding the CV changes that occur following ACLR, but there is emerging evidence to support a potential relationship between ACL injury and CV health. Previous data from our lab indicate that females with a history ACLR in the past 5 years have a higher percent body fat when compared to healthy matched controls, but they did not exhibit a difference in CRF as assessed by a cycle VO2max test. Steding-Ehrenborg et al. reported cardiac adaptations in athletes to the deconditioning and reconditioning associated with ACLR. They found that left and right ventricular volumes and total heart volume decreased with cessation of exercise following injury and then increased once endurance training was resumed. The increase in total heart volume also correlated with the concurrent increase in VO2peak of these athletes 6 months after resuming PA. A recent critically appraised topic also indicated that protracted cardiovascular impairments may be present after ACLR. A qualitative survey study showed an increased rate of arthritis and knee replacement surgery after an ACL injury. In addition, although statistical significance was not reached, there was a >50% increased rate of myocardial infarction in players with a
history of ACL tear. Almeida et al. reported that CRF was significantly reduced in professional soccer players with ACLR and aerobic function was not restored after 6 months of structured rehabilitation when compared to non-injured athletes of the same competitive level. Although the study by Almeida et al found that participants with a history of ACL injury had better cardiovascular outcomes compared with presurgical data, these individuals with history of ACL injury had less efficient cardiovascular systems compared with healthy controls. Lastly, it is becoming more obvious that individuals with ACLR exhibit reduced PA engagement patterns in the years following surgery, but we still do not fully understand how this reduction is impacting BMI, body composition, CRF, and other measures of CV health. Overall, evidence suggests that some CV impairments exist following ACLR, but the extent of these impairments and how long they may last is still unclear.

CONCLUSION

There is ample evidence supporting the role of PA, body composition, CRF, and arterial stiffness in long-term cardiovascular health among the general population, but limited evidence exists in individuals with ACLR. Because ACLR often occurs in young, active individuals, the introduction of a period of sedentary behavior during rehabilitation that can extend into the years following surgery may have a detrimental effect on this population. Due to the limited evidence regarding PA behavior, CRF, BMI, body composition, and arterial stiffness that is currently available in average adolescents and young adult individuals with ACLR, it is warranted to evaluate markers of CV health in
both the short- and long-term in this population. Through this dissertation project, further characterization of risk factors for CV health in individuals with ACLR will be explored.
CHAPTER 3: PHYSICAL ACTIVITY ENGAGEMENT OF ADOLESCENTS WITH
ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION
ABSTRACT

Adults with anterior cruciate ligament reconstruction (ACLR) are 2.5 times less likely to be active compared to uninjured individuals. Currently, it is unclear if physical activity (PA) engagement among adolescents 6 months post-ACLR is different compared to uninjured adolescents, how PA changes from 6 to 9 months following ACLR, and if these individuals are meeting PA recommendations of 60 minutes per day. PURPOSE: The purpose of this study is to compare time engaged in moderate-to-vigorous PA (MVPA) between adolescent individuals with and without a history of ACLR at two time points following surgery and over time. METHODS: Thirty-seven adolescents with primary, unilateral ACLR (25 F, months since surgery = 6.0±0.7, age= 15.9±1.3yrs) and 26 uninjured adolescents (13 F, age=14.9±1.5yrs) participated. PA was assessed using hip worn accelerometers for 7 days. Wear time (min/day) was validated using recommendations of Choi et al. and Evenson’s child cut points were utilized to categorize PA as sedentary, light, moderate, or vigorous. Time spent in MVPA (min/day) and step counts (steps/day) were compared between groups using separate one-way ANCOVAs with total wear time as a covariate. Change in MVPA and step count from 6 months to 9 months for adolescents with ACLR was assessed using a repeated measures ANCOVA. A Fischer’s exact test was used to compare frequency of meeting PA guidelines between groups. RESULTS: Adolescents post-ACLR had lower step counts when compared to uninjured participants at 6 months (p=0.015, ηp²=0.02) and 9 months (p=0.03, ηp²=0.12). No differences were observed at either timepoint following surgery as compared to the uninjured group for times spent at various levels of PA intensity. Adolescents with ACLR did not experience a change in MVPA (F(1,
16)=0.365, \(p=0.55, \eta_p^2=0.02\) or step count from 6 to 9 months \([F(1, 16)=1.92, p=0.18, \eta_p^2=0.11]\) Uninjured individuals were no more likely to meet PA recommendations than individuals with ACLR at 6 months and 9 months \((OR=1.33 [0.26, 6.94], p=1.00)\). Only 13.3\% \((2/15)\) of uninjured participants met step count guidelines, while no adolescents with ACLR achieved 10,000 steps per day at 6 months post-ACLR or at 9 months post-ACLR. **CONCLUSIONS**: Six and 9 months following ACLR, adolescents engage in similar MVPA volume when compared to their uninjured counterparts. Adolescents with ACLR also had lesser step counts than their uninjured peers and did not increase PA from 6 to 9 months following surgery. PA during adolescence can be predictive of PA participation across the lifespan and inadequate PA engagement can have detrimental effects on future health. Therefore, it is important to monitor and encourage PA engagement during adolescence, particularly in individuals returning to PA following ACLR.
INTRODUCTION

The United States Department of Health and Human Services (USDHHS) recommends that adults participate in 150 minutes of moderate-intensity aerobic activity per week\textsuperscript{59} and normative data suggests that 10,000 steps per day is an achievable goal for the healthy adult population.\textsuperscript{58} For children and adolescents, recommendations encourage participation in 60 minutes per day of moderate-intensity activity.\textsuperscript{59} Benefits associated with physical activity (PA) have been well-documented;\textsuperscript{56} yet many healthy individuals do not meet current PA recommendations.\textsuperscript{76} As of 2018, only 26% of adult men, 19% of adult women, and 20% of adolescents reported sufficient activity to meet the current aerobic and muscle-strengthening guidelines.\textsuperscript{59} Physical inactivity is an independent risk factor for mortality and morbidity\textsuperscript{59,135} and it is estimated to cause 9% of premature mortality.\textsuperscript{60} Although morbidities associated with physical inactivity become more apparent with age and are more prevalent in older populations, longitudinal studies have indicated that PA during childhood and early adulthood is a predictor of PA later in life.\textsuperscript{63,136,137} Therefore, events that occur early in life that limit or disrupt participation in PA may have consequences for health later.

Musculoskeletal injuries have been identified as a main factor that reduces PA participation.\textsuperscript{138,139} Among youth, sports are a main source of PA engagement, yet sports-related injuries are also the leading type of injuries experienced in this group.\textsuperscript{140} Anterior cruciate ligament (ACL) tears are a common and devastating knee injury for a young athlete\textsuperscript{141} and return to sport is a main goal following surgical reconstruction (ACLR).\textsuperscript{82} A recent systematic review and meta-analysis found that following ACLR (average 40 months post-surgery), 81% of patients resumed playing some form of
sport, 65% resumed their previous level of sport, and 55% returned to playing competitive sports.\textsuperscript{83} This decrease is concerning because studies have also reported a general pattern of declining PA participation from childhood to adolescence and sport is often the primary source of PA for young individuals.\textsuperscript{142} Therefore, those who cease sport participation due to injury or other barriers may be at elevated risk of becoming insufficiently active. Although many individuals eventually return to sport, post-ACLR rehabilitation requires a decrease in PA levels for at least the first 12 weeks, which is then followed by a progressive increase in activity until clearance at 6 to 9 months following surgery.\textsuperscript{6,7} Introduction of vigorous activity too early in rehabilitation could negatively affect the healing process and place the knee at risk for an adverse event such as reinjury or meniscus tear.

Previous investigations of device-measured PA among patients with ACLR have reported that independent of return to sport status, only 24% of adults with ACLR met the 10,000 steps per day recommendation and individuals with ACLR were 2.36x less likely to meet PA guidelines when compared to uninjured individuals.\textsuperscript{1} In adolescent female athletes with ACLR, no differences in MVPA were observed compared to uninjured athletes, but female athletes with ACLR did participate in fewer mean minutes per day of vigorous PA.\textsuperscript{9} Overall, it seems that some PA limitations persist throughout ACLR recovery in the population well beyond clearance for return to activity despite most patients stating a goal of returning to pre-injury PA level.\textsuperscript{82} It is assumed that PA will increase at the time of clearance for unrestricted PA (6-9 months) because of a desire to return to sport and activity, but clinicians and researchers do not know if this is actually the case based on limitations in the available literature.
Despite the recognized reductions in PA post-ACLR, there are a limited number of accelerometer-based assessments of PA in patients with ACLR and even less information about PA patterns among adolescents with ACLR. To date, there are also no prospective PA studies available that include adolescent patients during a time when they have recently transitioned out of clinical care (6-9 months post-ACLR). With rates of ACLR having increased over 60% in the last 20 years, particularly among adolescents, it is crucial that we consider how this surgical procedure and the period of inactivity associated with rehabilitation affects PA engagement in the months following surgery. This information can help to address potential PA interventions in this population. Currently, it is unclear how PA engagement among adolescents 6-9 months post-ACLR compares to uninjured adolescents and if they are achieving recommended PA guidelines. It is also unclear how PA engagement changes from 6 to 9 months following ACLR as these individuals should be reintegrating back into sport around this time. Therefore, the primary purpose of this study is to compare time engaged in moderate-to-vigorous PA (MVPA) between adolescent individuals with and without a history of ACLR at 6- and 9-months following surgery and over time. It is hypothesized that adolescents with ACLR will perform less MVPA at 6 and 9 months compared to a group of uninjured peers. It is also hypothesized that adolescents with ACLR will experience an increase in time spent in MVPA from 6 to 9 months following surgery.

METHODS

This was a prospective cohort study in which device-measured PA was assessed at two time points in a group of adolescent participants who were 6 months post-ACLR.
at enrollment and a group of uninjured, matched controls. Participants provided written informed consent or assent (accompanied by parental consent if <18 years of age) and were outfitted with and provided instructions for the appropriate use of a PA monitor. This study was approved by the Institutional Review Board at Michigan State University.

PARTICIPANTS

High school aged (13-18 years old) participants who were 6 months post-primary, unilateral ACLR and matched control participants were recruited from the university and surrounding community. All participants were free of any cardiopulmonary or neurological disease that would prohibit them from participating in MVPA. A health history questionnaire including both general medical history and knee specific injury history was used to monitor defined exclusion criteria and used for further data analysis. Participants who self-reported an associated medial collateral ligament injury and those who underwent a meniscal procedure at the time of ACLR were included. Participants who experienced a significant surgical complication resulting in a second surgical procedure, posterior cruciate ligament reconstruction, or extended medical care were excluded. Uninjured control participants were excluded if they had a history of significant lower extremity injury or any lower extremity surgery. Participants were matched between groups based on sex and age (±1 year).

PHYSICAL ACTIVITY MONITORING

Each participant was given a research-grade PA monitor (ActiGraph Link, Pensacola, FL) to wear for one week at two time points following surgery (6 and 9
months) (Table 2). Uninjured participants were also given PA monitors to wear for 7
days at one time point following enrollment in the study to be used as a control group.
Participants wore the accelerometer on the right hip over the anterior superior iliac
spine. Data were downloaded and screened for completeness and appropriate wear
time upon monitor return. A valid data collection period was considered to be a
minimum of 4 days of wear with no less than 8 hours per day. Participants were
asked to re-wear the monitor for an additional 7 day period if they did not achieve these
criteria. Participants were asked to remove the monitor for sleeping, bathing, and any
water-based activities.

The ActiGraph Link monitors collected data in raw acquisition mode after which
the data were processed and analyzed using ActiLife software (ActiGraph Corporation).
Wear time (minutes per day) was estimated and validated using the recommendations
of Choi et al. Evenson’s child cut points were then used to categorize PA as
sedentary, light, moderate, or vigorous based on the number of activity counts that
occurred per minute during the wear time. PA outcomes included mean minutes per
day of PA spent in light, moderate, vigorous, and MVPA. Percentage of time spent in
each intensity band during the wear-period was also calculated. Data were excluded
from analyses if the participant did not achieve the aforementioned criteria of 4 days
with at least 8 hours of wear time or if the participant did not wear the monitor for both
visits.
STATISTICAL ANALYSIS

Mean time per day spent in MVPA, sedentary, light, moderate, and vigorous activity and step counts were compared between the one wear period of the uninjured control group and the ACLR group at both 6 months and 9 months following surgery using a one-way ANCOVA with monitor wear time as the only covariate. Change in mean time per day spent in MVPA, sedentary, light, moderate, and vigorous activity, and step count from 6 months to 9 months for adolescents with ACLR was assessed using a repeated measures ANCOVA using monitor wear time as the covariate. Frequency of individuals in each group who met aerobic PA guidelines (60 mins/day of MVPA) and step count guidelines (10,000 steps/day) were calculated and a Fischer’s exact test was used to compare frequency of meeting guidelines between groups.

Partial eta squared effect sizes were calculated for each variable of interest to assess the magnitude of between-group differences. Effect sizes were classified as and small = 0.01, medium = 0.06, or large = 0.14 for $\eta^2$. Statistical significance was established a priori as $\alpha \leq 0.05$, and all analyses were performed using SPSS statistical software (v27; SPSS Inc, Chicago, IL).
Table 2. Accelerometer data collection and analysis methods.

<table>
<thead>
<tr>
<th>Items to Report</th>
<th>Methods</th>
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<tbody>
<tr>
<td>Model of accelerometer</td>
<td>Actigraph Link (GT9X)</td>
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<td>Data collection sampling rate</td>
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<td>Data analysis epoch length</td>
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<td>Place of accelerometer</td>
<td>Right ASIS (Hip)</td>
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<tr>
<td>Number of participants receiving accelerometer</td>
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<tr>
<td>Accelerometer distribution method</td>
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<td>Days of data collection</td>
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<td>Criteria for defining non-wear of accelerometer</td>
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<td>Small Window Length: 30 minutes</td>
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<td>interpretation method</td>
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<tr>
<td>Number of participants non-compliant or had</td>
<td>ACLR: 6 months - 9, 9 months - 18,</td>
</tr>
<tr>
<td>accelerometer malfunction issues</td>
<td>Uninjured: 6</td>
</tr>
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Abbreviations: ASIS = anterior superior iliac spine

RESULTS

Thirty-seven adolescents with primary, unilateral ACLR (25 female, months since surgery = 6.0 ± 0.7, age = 15.9 ± 1.3 yrs) and 26 uninjured adolescents (13 female, age = 14.9 ± 1.5 yrs) were enrolled in the study. Due to participant drop-out and invalid accelerometer wear time, a subgroup of only 19 adolescents with ACLR and 20 uninjured adolescents were included for analysis (Table 3). Participants with ACLR
were significantly older than their uninjured peers (p = 0.027), but no significant differences were observed for height, body mass, or body mass index (BMI) between groups (Table 3).

After controlling for amount of monitor wear time, adolescents 6 months post-ACLR had a significantly lower step count when compared to uninjured control participants (p=0.015, $\eta^2_p = 0.02$). This deficit in step count persisted at 9 months compared to uninjured controls (p=0.03, $\eta^2_p =0.12$) (Table 4). No differences were observed at either timepoint following surgery as compared to the uninjured control group for times spent at various levels of PA intensity (Table 4).

Adolescents with ACLR did not experience a significant change in mean PA over time from 6 to 9 months: MVPA minutes per day (F (1, 16) = 0.365, p = 0.55, $\eta^2_p = 0.02$), sedentary minutes per day (F(1,16) = 0.710, p =0.412, $\eta^2_p = 0.043$), light minutes per day (F (1, 16) = 0.025, p = 0.88, $\eta^2_p = 0.002$), moderate minutes per day (F (1, 16) = 0.651, p = 0.43, $\eta^2_p = 0.039$), or vigorous minutes per day (F (1, 16) = 0.033, p = 0.86, $\eta^2_p = 0.002$). Adolescents with ACLR also did not experience a significant change in mean steps per day from 6 to 9 months [F (1, 16) = 1.92, p =0.18, $\eta^2_p = 0.11$] (Figure 1).

Only 15.8% (3/19) of participants with ACLR at 6 months and 9 months and 20.0% (4/20) of uninjured individuals met PA recommendations. Uninjured individuals were no more likely to meet PA recommendations than individuals with ACLR at 6 months and 9 months (OR = 1.33 [0.26, 6.94], p = 1.00). Only 13.3% (2/15) of uninjured participants met step count guidelines, while no adolescents with ACLR achieved 10,000 steps per day at 6 months post-ACLR or at 9 months post-ACLR (p = 0.487). We did not calculate an odds ratio for this measurement because no adolescents with
ACLR met the recommendation. It is clear with a p-value = 0.487 that there was no difference between groups and uninjured participants were no more likely to achieve of 10,000 steps per day.

**DISCUSSION**

The purpose of this study was to compare PA engagement between adolescent individuals with a history of ACLR at two time points following surgery to a group of uninjured control adolescents and to evaluate change in PA over the 6 to 9 months following ACLR. It was hypothesized that adolescents with ACLR would spend less time engaging in MVPA as compared to their uninjured peers at each time point, but this was not the reality based on our findings. Individuals with ACLR at 6- and 9-months following surgery displayed statistically similar mean minutes per day spent in MVPA, sedentary, light, moderate, and vigorous activity as compared to their uninjured peers. These lack of differences in PA between groups are similar to findings from a study in young female athletes within 1-2 years following ACLR.\(^9\) Ezzat et al. reported mean MVPA times of 38.8 minutes per day in the injured group and 41.8 minutes per day in the control group.\(^9\) Overall, adolescents with a history of ACLR seem to be participating in similar amounts and intensities of PA as their uninjured peers; however, we cannot ignore that both groups are considered inactive based on the aerobic PA guideline of achieving 60 minutes of MVPA per day.

In addition to comparing PA participation between groups, it is also important to evaluate if these adolescents with a history of ACLR are participating in enough PA at an adequate intensity level. In 2017 it was reported that only 26.1% of all American
adolescents participated in sufficient activity to meet the current aerobic PA guidelines. On average, the overwhelming majority of participants in both groups fell short of achieving this recommendation while wearing the monitor (at least 8 hours). Uninjured individuals were no more likely to meet PA recommendations than individuals with ACLR at 6 months and 9 months (OR = 1.33 [0.26, 6.94], p= 1.00). Two out of the three participants with a history of ACLR who met recommendations at 6 months also met recommendations at 9 months. Because the 6-to-9-month timepoint following surgery is a time when patients are often cleared for full return to sports and activity, it was hypothesized that PA engagement would increase from 6 to 9 months in the ACLR group. Based on our results, we did not observe a significant increase in MVPA time or a significant change in any of the other PA variables assessed in this 3-month window. At 9 months following ACLR, these adolescent patients were still participating in MVPA for a similar amount of time as they were at 6 months post-ACLR. Less than half of the participants with ACLR (8/19) participated in a greater duration of daily MVPA at 9 months than they did at 6 months (Figure 2). This lack of improvement in PA from 6 to 9 months post-ACLR could be due to a number of factors including psychological barriers such as fear of returning to sport or fear of reinjury, or psychosocial barriers such as the loss of a role on a sports team or lack of access to a sports participation. Overall, this is surprising as we expected patients to be more comfortable engaging in more moderate and vigorous activity at 9 months post-ACLR and therefore to see a greater amount of time spent in MVPA as compared to 6 months post-ACLR.

We did not find any significant differences in the amount of time per day that participants spent in varying PA intensities when comparing adolescents with ACLR at 6
months versus uninjured adolescents, yet our effect sizes do indicate that there is a moderate effect for injury status on MVPA. Although not statistically significant, at 6 months post-surgery adolescents with ACLR participated in almost 10 minutes less MVPA per day as compared to their uninjured peers. This would equate to a difference in over 60 minutes of MVPA per week, which could be clinically significant for long-term health. It is possible that with a larger sample of participants we may be able to detect statistically significant changes, however, this information further supports the idea that clinicians and those involved in the rehabilitation process should promote PA to individuals with ACLR in this age group throughout recovery and the years following clearance for return to activity.

We did find that at 6 months post-surgery, participants with ACLR engaged in significantly fewer steps per day on average as compared to adolescents without a history of knee injury. Taking fewer steps per day is similar to previous findings in adult patients with ACLR as compared to an uninjured group of peers.\textsuperscript{1,2} Although it is recommended that adults take 10,000 steps per day, based on existing normative data, 60 minutes of MVPA is associated with 10,000-11,700 steps per day in adolescents.\textsuperscript{147} Only 13.3\% (2/15) of uninjured participants met these guidelines, while no adolescents with ACLR achieved 10,000 steps per day at 6 months post-ACLR or at 9 months post-ACLR (Figure 1). Uninjured individuals were no more likely to meet step count recommendations than individuals with ACLR at either 6 months or 9 months. These group percentages achieving 10,000 steps per day are also lower than what has been observed for adults with ACLR.\textsuperscript{1,2} One reason for this difference may be related to time since surgery. Previous studies have included participants who were on average further
out from surgery (27.8 ± 17.5 months\(^1\) and 33.0 ± 18.3 months\(^2\)) as opposed to our group of adolescents who may have still been transitioning out of clinical care and rehabilitation rather than fully having returned to sports and activity. Additionally, we hypothesize that type of PA engagement may also explain the reduced step counts of the adolescents in this study compared to adults. Walking and jogging may be more common forms of exercise for adults, which adolescents often times engage in sport rather than walking or jogging in their leisure time. Unfortunately, we do not have information about the type of PA that adolescents in this study were participating in to confirm this hypothesis. While this information gives us confidence that MVPA and step counts are related in this population, it is concerning that we are not seeing an increase in MVPA or step count during a time when most adolescents with ACLR should be returning to sport and increasing both PA time and intensity.

Although this is the first study to our knowledge to assess PA in an adolescent population of patients with ACLR and how it changes from 6 to 9 months following ACLR, there were a number of limitations present in the current investigation. There was high participant dropout among both groups at both timepoints which may have impacted our ability to get a clear view of adolescent PA engagement following ACLR and how it changes over time. Additionally, difficulty obtaining a sufficient number of adolescent participants’ PA data with monitor wear times of at least 10 hours forced us to use a minimum wear time of at least 8 hours instead, which is not ideal to capture a full day of activity. Due to the design of this study, we also do not know how active these adolescents with ACLR were prior to injury and it is possible that they were participating in less steps per day prior to ACLR. Lastly, part of this data set was collected during the
COVID-19 pandemic when lockdown procedures were in place, thus potentially affecting the ability of adolescents in both groups to freely participate in team sports activities. This could partially explain why only a small percentage of each group met recommendations for daily steps and daily MVPA.

**CONCLUSION**

The findings from this study indicate that the timepoint of 6 to 9 months following ACLR is not associated with reduced PA in adolescents when compared to uninjured peers. The majority of both adolescents with a history of ACLR and their uninjured peers displayed low levels of MVPA engagement and daily step counts that are not meeting recommendations. This study also highlights the importance of monitoring and encouraging PA engagement during adolescence. Given the long-term health implications of reduced or inadequate PA such as increased morbidity and mortality, a focus on increasing both PA time and intensity, particularly in individuals returning to PA following ACLR, should be a priority.
Table 3. Participant demographic information.

<table>
<thead>
<tr>
<th></th>
<th>ACLR n = 19</th>
<th>Uninjured n = 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>(5/14)</td>
<td>(10/10)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>15.9 ± 1.2*</td>
<td>14.9 ± 1.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.0 ± 12.6</td>
<td>169.0 ± 11.1</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>69.4 ± 19.7</td>
<td>65.6 ± 13.8</td>
</tr>
<tr>
<td>BMI (kg*m⁻²)</td>
<td>24.2 ± 5.4</td>
<td>22.7 ± 2.7</td>
</tr>
<tr>
<td>Time Since Surgery (mon.)</td>
<td>6.0 ± 0.7</td>
<td>-----</td>
</tr>
</tbody>
</table>

Values presented as mean±SD.
*P≤0.05.

Figure 1. Individual subject plot for steps per day for adolescents with ACLR at 6- and 9-months post-surgery.
Figure 2. Individual subject plot for MVPA per day for adolescents with ACLR at 6- and 9-months post-surgery.
Table 4. Physical activity of adolescents with ACLR at two timepoints post-surgery compared to uninjured peers.

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th></th>
<th>9 months</th>
<th></th>
<th>Uninjured</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACLR</td>
<td>P value</td>
<td>Effect Size $\eta_p^2$</td>
<td>ACLR</td>
<td>P value</td>
</tr>
<tr>
<td>Step Count (steps/day)</td>
<td>5947 ± 1961*</td>
<td>0.015</td>
<td>0.153</td>
<td>6057 ± 1574*</td>
<td>0.033</td>
</tr>
<tr>
<td>MVPA (mins/day)</td>
<td>33.8 ± 17.3</td>
<td>0.130</td>
<td>0.062</td>
<td>35.3 ± 16.8</td>
<td>0.283</td>
</tr>
<tr>
<td>Sedentary Time (mins/day)</td>
<td>592.6 ± 92.6</td>
<td>0.797</td>
<td>0.002</td>
<td>584.0 ±66.8</td>
<td>0.999</td>
</tr>
<tr>
<td>Light Time (mins/day)</td>
<td>167.5 ± 57.4</td>
<td>0.262</td>
<td>0.035</td>
<td>161.8 ± 41.4</td>
<td>0.168</td>
</tr>
<tr>
<td>Moderate Time (mins/day)</td>
<td>22.4 ± 9.9</td>
<td>0.172</td>
<td>0.051</td>
<td>24.0 ± 9.1</td>
<td>0.461</td>
</tr>
<tr>
<td>Vigorous Time (mins/day)</td>
<td>11.4 ± 8.4</td>
<td>0.167</td>
<td>0.052</td>
<td>11.3 ± 9.2</td>
<td>0.242</td>
</tr>
<tr>
<td>Total Monitor Wear Time (mins)</td>
<td>5550.1 ± 1862.3</td>
<td>---</td>
<td>---</td>
<td>5169.8 ±1892.8</td>
<td>---</td>
</tr>
</tbody>
</table>

Values presented as mean±SD.

*P≤0.05 indicates group difference between healthy and ACLR
CHAPTER 4: CHANGE IN BODY MASS INDEX FROM PRE- TO POST-SURGERY IN ADULTS AND ADOLESCENTS WITH ACLR
ABSTRACT

Physical activity (PA) participation can modulate weight status and body mass index (BMI). Previous studies have observed a reduction in PA following anterior cruciate ligament reconstruction (ACLR) and an increase in BMI has also been observed in patients post-ACLR. We do not fully understand how body weight and BMI may change from pre- to post-ACLR for adolescents and adults. **PURPOSE:** The purpose of this study was to assess change in body weight and BMI from pre-surgery to 6 months post-ACLR in adult and adolescent patients. **METHODS:** A retrospective chart review was conducted including adult and adolescent patients who underwent primary, unilateral ACLR and were previously enrolled in a prospective cohort study. BMI was calculated \(\text{[weight(kg)/height(m\(^2\)]}\) for all participants and BMI percentile was calculated for all participants under the age of 20 to account for changes in growth and maturation during adolescence. Pre-surgery to 6-months post-ACLR mean change in body mass, absolute BMI, and BMI percentile were also calculated and assessed using paired samples t-tests. Cohen’s d effect sizes were calculated to determine magnitude of change from pre- to post-ACLR. **RESULTS:** One hundred and 16 adolescents with ACLR (67 F; age =16.7±1.6yrs) and 63 adults (29 F; age=27.2±7.4yrs) participated. Adolescent participants experienced a significant increase in body mass (p<0.001), BMI (<0.01), and BMI percentile (p=0.02) from pre- to 6 months post-ACLR. Adult patients also experienced a significant increase in body mass (p<0.001) and BMI (p=0.006). **CONCLUSION:** Results from this study reflect an undesirable change to BMI in both adolescents and adults in the 6 months following ACLR. Revising rehabilitation to extend beyond traditional musculoskeletal strengthening to include focus on
incorporation and maintenance of healthy lifestyle behaviors related to diet and PA should be considered in order to help patients with ACLR to minimize the potential for negative long-term effects of weight gain following surgery.
INTRODUCTION

Approximately 250,000 anterior cruciate ligament (ACL) injuries occur in the United States each year.\textsuperscript{5} It has been reported that 81\% of patients who undergo surgical reconstruction resume playing some form of sport within 3 years of surgery.\textsuperscript{83} However, in the process of progressing from the time of surgery to an attempted return to sport, a lengthy recovery process involving outpatient rehabilitation and self-directed re-integration into unrestricted activities is needed in order to return to their desired level of physical activity (PA). The first 12 weeks following surgery consist of rehabilitation activities that are low intensity in order to allow for tissue healing and the avoidance of adverse events such as ACL graft failure.\textsuperscript{148} This is followed by a progressive increase in activity intensity, with the goal of eventual clearance for unrestricted activity beginning 6 to 9 months post-ACLR.\textsuperscript{148,149} Previous literature has noted that reduced PA levels may persist in this population well-beyond the transition back to normal activities.\textsuperscript{1–3} Not returning to sport may also result in the loss of an individual’s primary source of activity and for others to no longer consistently engage in appropriate levels of PA, yet return to sport is a goal of many patients following ACLR.\textsuperscript{82} These observed reductions in PA may indicate a disconnect between an individual’s desire to return to sport and their actual return to activity and PA participation.

PA level can have an impact on anthropometric measurements such as weight status and body mass index (BMI). A long break from regular PA can lead to a potential for weight gain. It is important that we consider adolescents and adults as separate populations when evaluating BMI change following ACLR due to the growth and maturation that occurs during adolescence. This is when the largest change in growth
and body composition occurs as an individual is experiencing a period of rapid growth. Significant differences exist between adult and pediatric patients with ACLR when using the standard equation \([\text{height (kg) / weight (kg)}^2]\) for calculating BMI values; therefore, it is difficult to compare adolescents with adults who have already achieved full maturation status. Instead, BMI for age percentiles should be used as the outcome of interest when evaluating change in an adolescent population as it allows for the comparison with normative data of other adolescents of the same sex and age. Results from a recent study showed that pediatric patients with a normal BMI underwent a statistically significant BMI increase during recovery from ACLR and failed to return to their presurgical BMI percentile even 2 years post-ACLR. Focusing on how BMI changes specifically in the adult population following ACLR is also important because it has been reported that there is a positive correlation between BMI and ACL revision surgery among adult patients. It is possible that ACLR may be an inciting event for post-surgical weight gain that can influence long-term health.

BMI is positively associated with various noncommunicable diseases including diabetes, high blood pressure, high non-HDL cholesterol, stroke, and ischemic heart disease. It has also emerged as a risk factor for musculoskeletal injuries and development of osteoarthritis. Previous literature examining trends in patients with a history of ACLR found that the proportion of overweight pediatric patients undergoing ACLR was significantly greater than the percentage of overweight individuals in the general population. There is also evidence that obesity is a risk factor for ACL reinjury and early ACL revision. Higher BMI has been reported as a consistent risk factor for poorer 6 year and 10 year patient reported outcomes for individuals with
ACLRT. Therefore, maintaining a BMI that is in a healthy range is an important for not only long-term joint health for the affected knee, but overall health. Current rehabilitation practices following ACLR\textsuperscript{6,148,149} are not focused on maintaining weight status or facilitating sufficient aerobic and resistance training exercises to support maintenance of body weight. Despite the documented reduction in PA following surgery\textsuperscript{1,3} and the increase in BMI that has been observed in patients post-ACLR,\textsuperscript{151} we do not have a clear picture of how body weight and BMI may change from pre- to post-ACLR when characterizing adolescents and adults, independently using best measurement practices. Therefore, the purpose of this study is to assess change in body weight and BMI from pre-surgery to 6 months post-ACLR in a diverse sample of patients. We hypothesized that body weight and BMI would increase significantly from pre- to 6 months post-ACLR similarly in both adolescents and adults.

**METHODS**

This was a retrospective chart review from patients previously enrolled in a prospective cohort study. Patients between the ages of 13 and 55 who underwent primary, unilateral ACL surgery between 2016 and 2020 at a university sports medicine clinic were included. Participants provided written informed consent or assent prior to enrolling in the study. This study was approved by the Institutional Review Board at Michigan State University.
ANTHROPOMETRIC MEASUREMENTS

Pre-surgical height and weight measurements were taken by clinical staff in the sports medicine office and obtained via chart review of medical records by a member of the research team. Standing height was measured to the nearest 0.1 cm using a stadiometer and body mass was measured to the nearest 0.01 kg using a beam balance. Post-surgical height and weight were measured at a follow-up laboratory testing date between 5- and 8-months following surgery in a research lab setting. If a patient had multiple follow-up measurements post-surgery, the testing session with a time since surgery closest to 6 months was selected for analysis.

CALCULATION OF BODY MASS INDEX

For all patients under the age of 20, BMI percentile for age was calculated from height and weight measurements taken prior to surgery and at the 6-month follow up lab visit. BMI percentile was determined by calculating BMI (Equation 1) and comparing it to the CDC growth charts which are based on normative data from the National Health and Nutrition Examination Survey (NHANES).

Equation 1. $\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2}$

BMI calculations were performed using RStudio Version 1.2.1335 (R Core Team, 2021) with the jBMI package (Birstler, 2016). BMI percentile is used to account for normal changes in BMI for adolescents during growth. Change in BMI percentile relative to initial BMI at the time of surgery was also calculated for each patient under the age of 20. BMI categorizations were assigned based on Centers for Disease Control and Prevention guidelines for BMI percentiles: less than the 5th percentile were
categorized as underweight, 5th to less than the 85th percentile were categorized as normal weight, 85th to less than 95th percentile were considered overweight, and 95th percentile and above were categorized as obese.

For all adult patients (≥ age 20), BMI was calculated and absolute change in BMI relative to initial BMI at the time of surgery was also calculated. For adult patients, the following cut points were used: less than 18.5 kg/m$^2$ was considered underweight, 18.5 to 24.9 kg/m$^2$ was considered normal or healthy weight, 25.0 to 29.9 kg/m$^2$ was considered overweight, and greater than 30.0 kg/m$^2$ was categorized as obese.

**STATISTICAL ANALYSIS**

Means and standard deviations were calculated for all demographic variables of interest. Change in absolute BMI for adults and change in BMI percentile for adolescents from pre- to post-ACLR were assessed using paired samples t-tests. Cohen’s $d$ effect sizes were calculated to determine the magnitude of change from pre-to post-ACLR. Effect sizes were then categorized using Cohen criteria: large $\geq 0.5$, medium $\geq 0.3$, and small $\geq 0.1$. Statistical significance was established a priori as $\alpha \leq 0.05$, and all analyses were performed using SPSS statistical software (v27; SPSS Inc, Chicago, IL).

**RESULTS**

One hundred sixteen adolescents with ACLR (67 female, 49 male, mean age = 16.7 ± 1.6 years) and 63 adults (29 female, 34 male, mean age = 27.2 ± 7.4 years) participated. Among adolescent patients there was a significant increase in body mass
Effect sizes indicate there is a large effect for time on body mass change ($d = 0.52 \ [0.32 \text{ to } 0.72]$), a moderate effect for time on BMI ($d = 0.42 \ [0.23 \text{ to } 0.61]$), and a small effect for time on BMI percentile ($d = 0.22 \ [0.03 \text{ to } 0.40]$). Adult patients also experienced a significant increase in body mass ($p < 0.001$) and BMI ($p = 0.006$) pre- to post-ACLR (Table 2). Effect sizes indicate a moderate effect for time on both body mass ($d = 0.47 \ [0.21 \text{ to } 0.73]$) and BMI ($d = 0.36 \ [0.10 \text{ to } 0.61]$).

**DISCUSSION**

This retrospective chart review evaluated the change in body weight and BMI from pre-surgery to 6 months post-ACLR in adolescent and adult patients. Our hypotheses that body weight and BMI would significantly increase from pre-surgery to 6 months post-ACLR were confirmed. This equates to an increase in BMI of about 0.5 kg/m$^2$ and an increase in body mass of 2.0 kg for adults with ACLR. For adolescent patients with ACLR, this equates to a 2.0 percentile increase in BMI percentile and a 2.0 kg increase in body mass. These findings highlight the potential consequences that may arise due to ACLR and restrictions of PA during rehabilitation. ACLR may lead to decreased PA and weight gain, initiating a cycle of injury, sedentary lifestyle, weight gain, and increased long-term risk for musculoskeletal problems and/or non-communicable diseases such as CV disease.$^{156}$

Our results are similar to previous literature examining BMI change following ACLR.$^{2,9,91,151}$ The effect sizes in this study for adolescents indicate the effect of time on BMI percentile were small and large, respectively with 95% confidence intervals that do
not cross zero. MacAlpine et al. reported that adolescents tended to experience an increase in BMI percentile following surgery, with a median increase of 1.83 percentile points peaking at around 6 months post-surgery. This trend and the magnitude of this change are similar to the findings in our adolescent group. While we did not evaluate change based on BMI percentile classifications in this study, MacAlpine et al. found that adolescents who were part of the normal weight group (5-85th percentile) had significantly larger changes in BMI percentile than other groups following surgery, peaking at a median percentile increase of 4.15 percentile points at 9 months post-surgery.\textsuperscript{151} Results from another study examining changes in BMI and body composition during maturation in female athletes of a similar age also reported elevated BMI in the first year following a knee injury. In those who reported a knee injury, they experienced significantly greater increases in BMI percentile (by up to 5 points more) relative to their uninjured peers. These young female participants also had an increase in body fat percentage by up to 1.5\% as compared to their uninjured peers.\textsuperscript{94} Considering these findings from previous studies and our results that observe an increase in BMI within the first 6 months following ACLR, it is possible, yet speculative, that adolescent participants in this study may continue to gain weight and experience a further increase in BMI percentile as they approach 9 to 12 months following surgery.

Although we observed an increase in BMI percentile for adolescents, BMI percentile classification remained relatively stable. The majority of adolescents with ACLR in this study were considered to be in a healthy BMI percentile (5-85th) both pre-surgery (84/116 patients) and post-ACLR (82/116 patients). However, 15.5\% (18/116) were classified as overweight (85-95th percentile) and 10.3\% (12/116) were classified as
obese prior to surgery with a slight shift to 13.8% (16/116) of adolescents being considered overweight and 12.9% (15/116) considered obese after ACLR. These percentages are similar to previously reported proportions of pediatric patients with ACLR with BMIs placing them in the overweight (26.4%) and obese (9.3%) categories. Unfortunately, we do not have control data from participants with no history of injury in this study; but in general, there is a trend of increasing prevalence of obesity in pediatric, adolescent, and adult populations as they age. The National Center for Health Statistics reported that based on 2017-2018 data that 16.1% of children ages 2-19 were considered overweight and 19.3% were considered obese in the general population, with more specifically 21.2% of adolescents aged 12 to 19 years old being considered obese.

In adult patients a moderate effect of time from pre- to post-surgery with a significant confidence interval was detected for both BMI and body weight. Compared to adolescent patients, a similar shift in BMI classifications were observed from pre-surgery to post-ACLR in adult patients. Prior to surgery, 39.7% (25/63) were classified as overweight (≥25kg/m\(^2\)) and 15.9% (10/63) as obese (≥ 30 kg/m\(^2\)), which increased to 42.9% (27/63) categorized as overweight and 19.0% (12/63) as obese at 6 months following surgery. In 2017-2018, the prevalence of obesity among adults over age 20 in the US general population was reported as 42.5%, with 73.6% of adults being considered overweight or obese. While it is concerning that the percentage of adolescents and adults who were considered overweight or obese increased from pre-surgery to post-ACLR in this study, these percentages are below the prevalence of obesity in the general population, which is encouraging. It is likely that many of the
individuals in this study were athletes prior to injury and this could explain the lower prevalence of obesity. However, the small number of individuals who moved into a worse BMI classification does highlight a small, but meaningful issue in this population.

BMI greater than 25.0 kg/m² is associated with an elevated risk of ACL injury. Additionally, patients with elevated BMI are more likely to require additional surgery at the time of primary ACLR and BMI greater than 25.0 kg/m² has also been cited as a risk factor for early ACL revision. While a mean percentile shift of 2.0 points in adolescents and a mean increase in BMI by 0.5 kg/m² in adults may not sound like a clinically significant change, both groups did experience a mean increase in body mass by about 2.0 kg. This would correspond with a 3.4% and 2.4% increase in body mass from pre-surgery for adolescents and adults, respectively. Previous studies have reported a range of 2% to 20% weight reductions as a clinically important difference in weight loss that can have an impact on CV disease risk parameters and health related quality of life measures in obese patients. Taken together, we can make the assumption that a significant weight gain would have the opposite effect and place an individual at greater risk for long-term poor health outcomes. The evidence from this study helps to further support the necessity of evaluating BMI and its change throughout the ACLR rehabilitation process.

This study has several limitations due to the retrospective nature of its design. Pre-surgical height and weight measurements were not taken by the research team and thus could be subject to human error with different clinical staff recording these measurements. In the adolescent group, it is possible that weight gain attributed to normal growth and development may influence and contribute to part of the increase in
BMIs we are observing over time. However, without an indicator of maturation status of these adolescent individuals we are limited in our ability to quantify the magnitude of this change due to normal growth and maturation. We also cannot go without mentioning that while BMI is a simple calculation and clinically applicable quantification of body size in large sample sizes, it is considered a proxy measure of adiposity and thus is limited because it fails to differentiate between fat mass and fat-free mass. Depending on height, individuals with high lean mass may be classified as overweight or obese, but have low or normal fat mass. A recent study in adult women with a history of ACLR showed that women with ACLR had a higher percent body fat than women without a history of injury. We did not evaluate body composition in this study and thus cannot comment on the health classifications of these participants based on body composition. It is possible that based on our results, the small, yet significant, change in weight status may be driven by a loss of lean tissue (muscle mass) that has been replaced with fat. This is an important limitation of BMI to acknowledge because of the negative associations that exist between high fat mass and poor health outcomes. Despite the limitations, this study analyzed a large sample size of individuals with ACLR that included a wide age range that was analyzed using both BMI and BMI percentiles and contributes to the existing literature in assessing change in anthropometric characteristics following ACLR.

**CONCLUSION**

Overall, the results from this study reflect an undesirable change to BMI in both adolescents and adults following ACLR. The question as to how much weight gain and
what kind of weight gain (lean mass vs. fat mass) is hazardous still remains unanswered, but BMI is a modifiable risk factor that is easily measured and feasible to track throughout rehabilitation. Revising rehabilitation to extend beyond traditional musculoskeletal strengthening to include focus on incorporation and maintenance of healthy lifestyle behaviors related to diet and PA should be considered in order to help patients with ACLR to minimize the potential for negative long-term effects of weight gain following surgery.
Table 5. Adolescent participants’ change in anthropometrics from pre- to post-ACLR.

<table>
<thead>
<tr>
<th></th>
<th>Pre-ACLR</th>
<th>Post-ACLR</th>
<th>p-value</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohen's d [95% CI]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.87 ± 0.09</td>
<td>173.32 ± 0.09</td>
<td>0.08</td>
<td>0.17 [-0.2 to 0.35]</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>70.07 ± 15.13</td>
<td>72.42 ± 16.88</td>
<td>&lt; 0.001*</td>
<td>0.52 [0.32 to 0.72]</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>23.31 ± 3.80</td>
<td>23.98 ± 4.39</td>
<td>&lt;0.01*</td>
<td>0.42 [0.23 to 0.61]</td>
</tr>
<tr>
<td>BMI Percentile</td>
<td>65 ± 25</td>
<td>67 ± 25</td>
<td>0.02*</td>
<td>0.22 [0.03 to 0.40]</td>
</tr>
<tr>
<td>Time Since Surgery (mo.)</td>
<td>----</td>
<td>6.17 ± 0.65</td>
<td>----</td>
<td></td>
</tr>
</tbody>
</table>

Values presented as mean±SD unless otherwise indicated. ACLR, anterior cruciate ligament reconstruction; *P<0.05

Table 6. Adult participants’ change in anthropometrics from pre- to post-ACLR.

<table>
<thead>
<tr>
<th></th>
<th>Pre-ACLR</th>
<th>Post-ACLR</th>
<th>p-value</th>
<th>Effect Size</th>
</tr>
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<tr>
<td></td>
<td>Cohen's d [95% CI]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174.25 ± 11.17</td>
<td>174.72 ± 10.71</td>
<td>0.11</td>
<td>0.20 [-0.05 to 0.45]</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>80.19 ± 19.94</td>
<td>82.09 ± 20.08</td>
<td>&lt;0.001*</td>
<td>0.47 [0.21 to 0.73]</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>26.14 ± 4.54</td>
<td>26.66 ± 4.87</td>
<td>0.006*</td>
<td>0.36 [0.10 to 0.61]</td>
</tr>
<tr>
<td>Time Since Surgery (mo.)</td>
<td>----</td>
<td>6.43 ± 0.70</td>
<td>----</td>
<td></td>
</tr>
</tbody>
</table>

Values presented as mean±SD unless otherwise indicated. ACLR, anterior cruciate ligament reconstruction; *P<0.05
CHAPTER 5: CARDIOVASCULAR HEALTH OF INDIVIDUALS WITH ACLR
ABSTRACT

PURPOSE: The purpose of this study was to compare body composition, cardiorespiratory fitness (CRF), arterial stiffness, and physical activity (PA) engagement between individuals with ACLR and uninjured controls. METHODS: Sixteen individuals with ACLR (months since surgery=36.3 ±19.0; age=21.8±3.2 years) and 8 uninjured individuals (age=22.8 ± 3.5yrs) matched based on age (±1yrs), sex, and Tegner Activity Level (±1) participated. Body fat percentage (%BF) was estimated using air displacement plethysmography, CRF was assessed via a graded treadmill test, arterial stiffness was assessed using carotid-to-femoral pulse wave velocity (cfPWV), and PA was assessed using accelerometers worn for 7 days. Groups were compared using Mann-Whitney U tests. Time (mins/week) spent in moderate-to-vigorous PA (MVPA) and step count (steps/day) were compared between groups using a one-way ANCOVA with 7-day total wear time as the only covariate. RESULTS: Individuals with a history of ACLR had greater body mass (p=0.01), BMI (p<0.01), and fat mass (p=0.02) compared to uninjured individuals. No differences were observed for %BF (p=0.19), fat free mass (p=0.07), MVPA (mins/week) (p=0.28) or daily step count (p=0.38) between groups. Participants with a history of ACLR had significantly shorter treadmill time to exhaustion as compared to uninjured participants (p=0.04). There were no differences observed between groups for VO\textsubscript{2peak} (p=0.24), max HR (p=0.70), max lactate (p=0.70), peak SBP (p=0.79), or arterial stiffness (cfPWV) (p=0.97). CONCLUSION: This study indicates that individuals with ACLR display similar characteristics of CV health as their uninjured peers, but those with ACLR may experience elevated BMI and fat mass and end a maximal graded exercise test sooner. The time following ACLR presents an
opportunity for researchers and clinicians to promote healthy behaviors and these results also demonstrate the continued need for consideration of PA and diet during clinical care to ensure that ACLR does not become a risk factor for CVD.
INTRODUCTION

Approximately 250,000 anterior cruciate ligament (ACL) injuries occur each year in the United States, which results in more than 125,000 ACL reconstructions (ACLR) being performed annually.\(^5\) ACL injuries and ACLR are most likely to happen to individuals under age 30 and rates of ACLR have increased over 60% in the last 20 years.\(^4,5\) ACLR typically requires 6 to 9 months of recovery time, during which patients are largely limited to light activity for the first 12 weeks after surgery followed by a slow progression of activity intensity throughout the rehabilitation process.\(^162,163\) A recent study showed that independent of return to sport status, individuals with ACLR were 2.36x less likely to meet United States Department of Health and Human Services (USDHHS) recommendations for weekly PA when compared to healthy individuals.\(^1\) This is contrary to the goal of the ACLR procedure and the desire of many patients to return to sport.\(^82\)

Decreased PA volume and intensity in individuals with ACLR is especially concerning because it has been well-established that physical inactivity is a risk factor for various chronic diseases such as type II diabetes, hypertension, coronary heart disease, and some cancers.\(^60\) It is possible that if individuals are less active following ACLR, this may lead to weight gain, unfavorable change in BMI,\(^93\) increased fat mass,\(^2\) and a potential for detrimental effects to long-term cardiovascular (CV) health.\(^59\) In addition to evaluating body composition and CRF to evaluate CVD risk, assessment of carotid-to-femoral pulse wave velocity (cfPWV) can provide important information about CV health. cfPWV has been used to measure arterial stiffness, or the elasticity of the arterial wall, which has been recognized as an independent marker of CVD\(^122\) whereby
increased arterial stiffness is linked to an increased risk of CVD and mortality. The amount of time spent in both light and moderate PA is associated with lower arterial stiffness, while sedentary behavior is associated with higher arterial stiffness.\textsuperscript{127} Arterial stiffening increases peripheral wave reflection, leading to an increase in ventricular afterload, a reduction in coronary perfusion, and myocardial hypertrophy and ischemia.\textsuperscript{129,130} While most research in this area is among older individuals, it is possible that young people who exhibit sedentary behavior, such as those who are rehabilitating an injury may also develop increased arterial stiffness. Among elderly patients, there is evidence of lower cfPWV in individuals who walked 10,000 steps per day compared to walking 6,000 steps per day.\textsuperscript{131} There is also evidence that PA is inversely related to PWV and sedentary time is positively associated;\textsuperscript{128} therefore, it is important to consider encouragement of aerobic exercise training as a means to increase PA and improve CV health of individuals with ACLR.

The apparent negative effects of ACLR on PA participation should also be considered given that consistent participation in PA is the strongest predictor of cardiorespiratory fitness (CRF)\textsuperscript{13} and because return to sport participation is a goal for the majority of patients with ACLR.\textsuperscript{82} It is understood that individuals with low CRF have a higher risk of CV disease (CVD), all-cause mortality, and mortality attributable to various cancers.\textsuperscript{13} Unfortunately, limited information is available regarding CRF profiles following ACLR in young adults who are not classified as elite athletes. Almeida et al. reported that CRF was significantly reduced in professional soccer players with ACLR and aerobic function was not restored after 6 months of structured rehabilitation,\textsuperscript{104} but it is challenging to generalize these findings to a non-elite athlete population. In the only
study to investigate these variables among non-elite athletes, absolute VO\textsubscript{2peak} during a cycle graded exercise test was similar among a small sample of women with ACLR and healthy individuals. However, when accounting for body mass, individuals with ACLR had a significantly lower relative VO\textsubscript{2peak}. This difference in relative CRF was most likely due to significantly higher % body fat and fat mass in the women with ACLR rather than a true difference in CRF.\textsuperscript{2} These results highlight the potential for the further need to assess CRF in both men and women a more diverse sample of individuals with ACLR.

Despite the recognized reductions in PA post-ACLR, there are a limited number of accelerometer-based assessments of PA in this population\textsuperscript{1,3,8} and it is unclear how recovery from ACLR affects body composition, CRF, and other CV outcomes following surgery and rehabilitation. With rates of ACLR having increased over 60% in the last 20 years,\textsuperscript{4,5} it is crucial that we consider how this surgical procedure and the period of inactivity that is associated with rehabilitation affects these CV health outcomes in the years following surgery in order to address potential interventions in this population. Therefore, the purpose of this study was to characterize and compare body composition, CRF, device-measured MVPA, and cfPWV (arterial stiffness) between individuals with a history of ACLR and uninjured, matched control participants with no history of lower extremity injury. It was hypothesized that individuals with a history of ACLR would have poorer CV health than individuals without a history of ACLR.

METHODS

This was a cross-sectional study in which CV outcomes were measured in a group of participants with a history of ACLR in the previous 6 years and a group of
uninjured, matched control participants. This study was approved by the Michigan State University Institutional Review Board for human subjects research and all participants provided written informed consent prior to study participation. Participants completed two study visits and were given a PA monitor to wear during the 7 days between visits. Visit 1 consisted of a body composition assessment via air displacement plethysmography (BodPod) and a measurement of arterial stiffness via cfPWV. The participants completed the discontinuous, graded treadmill test during visit 2.

PARTICIPANTS

A total of 16 participants with a history of unilateral ACLR and 8 matched control participants were recruited from the university and surrounding community. All participants were 18-30 years old and apparently free of any cardiopulmonary or neurological disease that would prohibit them from participating in moderate-to-vigorous PA (MVPA). A health history questionnaire including both general medical history and knee specific injury history were used to monitor for defined exclusion criteria and used for further data analysis. Participants in the ACLR group were recruited to include active men and women who had undergone unilateral, primary ACLR in the past 6 years and had been fully cleared to return to PA by a medical professional. Participants who self-reported an associated medial collateral ligament injury and those who underwent a meniscal procedure at the time of ACLR were included. Participants who experienced a significant surgical complication resulting in a second surgical procedure, posterior cruciate ligament reconstruction, or extended medical care were excluded. Uninjured control participants were excluded if they had a history of significant lower extremity
injury requiring surgery. Participants were matched across groups based on sex, age (±1 year), and self-reported Tegner Activity Level (±1 level).64

PATIENT-REPORTED PHYSICAL ACTIVITY LEVEL

Participants completed valid and reliable patient-reported outcome measures at the end of the testing session using an online survey platform (Qualtrics). The Tegner Activity Level Scale was used to evaluate and match participants based on self-reported PA level.64

BODY COMPOSITION

All participants were instructed to avoid exercising or eating 3 hours prior to the assessment. Participants wore spandex shorts, a sports bra for women, and a hair cap to ensure accurate body composition estimation. Standing height was measured to the nearest 0.1 cm using a wall-mounted, calibrated stadiometer. Body mass was measured to the nearest 0.01 kg using a calibrated beam balance. Body mass index (BMI) was calculated as body mass (kg) divided by height (m) squared. Body volume was measured via air displacement plethysmography using a BodPod (COSMED, Chicago, Illinois). Using body mass and volume measurements, each participant’s body density was calculated and converted to % body fat using the modified Siri equation.99 Fat mass (kg) and fat free mass (kg) were determined using % body fat and the participant’s body weight. The BodPod was calibrated with a cylinder of known volume before testing, and thoracic gas volume was predicted. Previous research has shown that the BodPod provides a valid estimation of body fatness in the general population.98
PHYSICAL ACTIVITY MONITORING

At the end of the first study visit, each participant was given a research-grade PA monitor (ActiGraph Link, Pensacola, FL) to wear for one week following the testing session (Table 1). Participants wore the accelerometer over the right anterior superior iliac spine for the 7 days. Monitors were returned at the second study visit which took place at least 1 week later. Data was downloaded and screened for completeness and irregularities at the second study visit. A valid data collection period was considered to be a minimum of 4 days (3 week days and 1 weekend day) of wear with no less than 10 hours per day. Participants were asked to re-wear the monitor for an additional full 7 day period following study visit 2 if they did not achieve these criteria. Participants were asked to remove the monitor for sleeping and bathing.

The ActiGraph Link monitors were used to collect data in raw acquisition mode after which the data were processed and analyzed using ActiLife software (ActiGraph Corporation). Wear time (minutes per day) was estimated and validated using the recommendations of Choi et al. Troiano adult cut-points were then used to categorize PA into light, moderate, vigorous, or very vigorous based on the number of activity counts that occurred per minute during the wear time. The primary PA variables assessed were the volume of MVPA (in minutes per week) and the number of steps (steps per day) completed by the participants during the wear-period. The amount of time (minutes per week) spent in MVPA was calculated based on these cut-points.
CARDIORESPIRATORY FITNESS MEASUREMENT

A discontinuous, treadmill (Trackmaster TMX425C, Newton, KS, USA) graded exercise test utilizing a modified version of the Bruce Protocol\(^{103}\) was performed by all participants to evaluate differences in CRF. Prior to testing, a resting heart rate and seated BP were taken. Respiratory gases were collected in 20 second sampling periods using a metabolic cart (ParvoMedics TrueOne 2400, Sandy, UT, USA). Heart rate was monitored continuously using a Polar heart rate monitor (Polar Team Pro System, Finland) and documented at the middle and end of each 3-minute stage. A 60-second rest period was included after each stage where the participant stepped onto the running board to allow for blood collection via fingerstick to determine blood lactate at the end of each stage. Participants reported subjective evaluation of exertion levels 2-minutes into each exercise stage using the 15-point version of the Borg Rating of Perceived Exertion (RPE) scale (minimal effort = 6; maximum effort = 20). The test was terminated when participants reached volitional exhaustion and stopped running or when the test was ended by the test administrator due to safety concerns. The primary outcome of this assessment was VO\(_{2}\)\(_{\text{peak}}\) (highest 20 second VO\(_2\) value). To ensure validation of the test and that appropriate effort was given, achievement of two of the following criteria were used: plateau in VO\(_2\) (<2ml/kg/min), heart rate ≥95% of age-predicted maximum, peak respiratory exchange ratio (RER) (VO\(_2\)/VCO\(_2\)) ≥1.10, maximal blood lactate >8 mmol/L, or RPE >17.\(^{117}\)

BLOOD LACTATE MEASUREMENT DURING EXERCISE

Baseline blood lactate was measured using a portable blood lactate analyzer
(Lactate Plus)$^{164,165}$ prior to beginning the CRF test. Blood lactate measurements were taken via fingerstick during the 60-second rest period at the end of each 3-minute stage during the discontinuous graded exercise test. Additional measurements were taken at the completion of the test and five minutes post-testing. Measurements were used to establish the stage during which onset of blood lactate occurred (OBLA) (4mmol/L) and for determination of lactate threshold, the stage at which lactate begins to accumulate in the blood faster than it can be cleared. Lactate maximum (mmol/L) was determined by the highest blood lactate measurement.

**CAROTID-TO-FEMORAL PULSE WAVE VELOCITY**

Prior to the study visit, the participants were instructed to abstain from consuming nicotine products (i.e., smoking, vaping or chewing) for 1 hour, food or drink for 4 hours (water was okay), caffeine and alcohol for 12 hours, exercise for 24 hours, and to take all medications and vitamins as usual to ensure measurement accuracy. The participant was instructed to lay in the supine position quietly in a dimly lit room for 10 minutes, after which, four blood pressure measurements were taken at 1-minute intervals using an automated sphygmomanometer (Dinamap Carescape V100; GE Healthcare, Buckinghamshire, UK). Resting BP can influence cfPWV, therefore it was collected to ensure if differences in resting BP existed between groups they would be controlled for in our comparisons. Following this, cfPWV was assessed using a hand-held tonometer (Model SPT-301; Millar Instruments Inc.) and data acquisition system (Powerlab 8/35, AD Instruments Ltd) and its proprietary software (LabChart 8, AD Instruments Inc.). Arterial pressure waveforms were sequentially collected for a minimum of 30 s from the
right common carotid artery and right femoral artery by applying the tonometer to the surface of the skin using a light pressure. Throughout the assessment heart rate was recorded using a single-lead electrocardiogram (Model ML-132; AD Instruments Ltd.). The distance between the carotid and femoral arterial measurement sites were measured along the surface of the body using a measuring tape.

cfPWV is defined as the speed of travel of the pulse between the carotid and femoral arterial sites\textsuperscript{125} and is calculated using the equation $\text{cfPWV} = (0.8 \times \text{distance}) \div \Delta t$. The pulse transit time ($\Delta t$) is the difference between the carotid pulse transit time and the femoral pulse transit time; this is calculated as the time delay between the R-spike of the ECG signal and the arrival of the arterial pressure waveform at each arterial site. To determine the arrival of the waveform at each site, arterial pressure waveforms were band-pass filtered (2-30 Hz)\textsuperscript{126} and the minimum value of the filtered signal was identified as the arrival of the waveform. A cfPWV was calculated using 10 s data sections and the reported value is the average of two, 10 s sections. If the difference between these two values was $>0.5$ m/s, a third 10 s data section was analyzed and the median of the three values was reported.\textsuperscript{124}

**STATISTICAL ANALYSIS**

Means and standard deviations of all groups were calculated for each variable of interest. In consideration of a small unequal sample size in both groups, a Shapiro-Wilk’s test ($p> 0.05$) and a visual inspection of histograms showed that variables of interest were not normally distributed, requiring the use of a non-parametric test. Separate Mann Whitney U tests were used to identify between group (ACLR and
uninjured control) differences for BMI, % body fat, relative VO\textsubscript{2peak}, lactate maximum, and cfPWV. Partial Eta Squared effect sizes were calculated using the equation ($\eta^2 = \frac{z^2}{N}$) for nonparametric data. Resting BP was also compared between groups; if differences existed, resting BP was controlled for in our assessment of cfPWV. Device-measured PA, time (minutes per week) spent in MVPA, %MVPA time, and daily step count (steps per day), were compared between groups using a one-way ANCOVA after controlling for 7-day total wear time (minutes) as the only covariate. Partial Eta Squared ($\eta^2$) effect sizes were calculated for all PA variables of interest to determine magnitude of between-group differences. Effect sizes were classified as small = 0.01, medium = 0.06, or large = 0.14 for $\eta^2_{\text{p}}$.\textsuperscript{144} Statistical significance was established a priori as $\alpha \leq 0.05$, and all analyses were performed using SPSS statistical software (v27; SPSS Inc, Chicago, IL).
<table>
<thead>
<tr>
<th>Items to Report</th>
<th>Methods</th>
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<tr>
<td>Model of accelerometer</td>
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<td>Data analysis epoch length</td>
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<td>Place of accelerometer</td>
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<td>Spike Tolerance: 2 minutes&lt;sup&gt;73&lt;/sup&gt;</td>
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<td>analysis</td>
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<td>Accelerometer data PA outcome of interest and</td>
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<tr>
<td>interpretation method</td>
<td>Cut points and MVPA: Troiano (2008)&lt;sup&gt;76&lt;/sup&gt;</td>
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<tr>
<td>Number of participants non-compliant or had</td>
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<tr>
<td>accelerometer malfunction issues</td>
<td>Uninjured: 0</td>
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Abbreviations: ASIS = anterior superior iliac spine
RESULTS

Sixteen individuals with ACLR (6 male, 10 female) and eight participants without a history of injury (1 male, 7 female) participated in this study. Demographic information is presented in Table 8. When comparing anthropometric measurements between groups, individuals with a history of ACLR had significantly greater body mass (p=0.01), BMI (p<0.01), and fat mass (p=0.02) as compared to individuals without a history of injury (Table 3). Effect sizes indicate a large effect for injury status on body mass, BMI, and fat mass. No differences were observed for percent body fat (p=0.19) or fat free mass (p=0.07) between groups (Table 9). We were unable to obtain body composition results on one uninjured participant (female, age 19) due to lab shut down during COVID-19 and one participant with ACLR (male, age 24) due to measurement issues. No significant differences in mean MVPA time per week, percentage of wear time, or mean daily step count were observed between groups (Table 10).

All participants achieved the necessary criteria to ensure validation of the maximal exercise test and that appropriate effort was given. During the maximal treadmill exercise test, participants with a history of ACLR had significantly shorter time to exhaustion as compared to uninjured participants (p=0.04). There were no differences observed between groups for VO_{2peak} (p=0.24), maximal HR (p=0.70), maximal lactate (p=0.70), or peak SBP (p=0.79) during the test. Additionally, there were no significant differences in arterial stiffness (cfPWV) observed between groups (p=0.97) (Table 11).
DISCUSSION

The results from this study help to further expand our understanding of CV health outcomes and PA engagement in young individuals with a history of ACLR. We hypothesized that individuals with ACLR would have overall poorer CV health profile than individuals without a history of ACLR; including greater percent body fat, lesser MVPA engagement, lower CRF, and higher cfPWV indicating greater arterial stiffness as compared to their uninjured peers. However, the results of this study did not fully support our hypotheses. Individuals with ACLR did have significantly greater BMI and fat mass and ended the graded treadmill test earlier than uninjured individuals, but participants with ACLR displayed similar anthropometric characteristics, CRF, PA engagement, and arterial stiffness as compared to their uninjured peers.

Individuals with a history of ACLR had significantly greater body mass, BMI, and fat mass as compared to individuals without a history of injury (Table 3). However, due to the nature of this cross-sectional study, it is possible that these individuals may have had a greater body mass and fat mass prior to injury. Unlike previous research where a group of women with ACLR had on average 10.1% more body fat than healthy, matched controls, no differences were found with respect to percent body fat between groups in the present study. On average, individuals with ACLR in our study did have greater percent body fat (26.5 ± 8.4%) than individuals without a history of ACLR (21.5 ± 5.3%), but these results were not statistically significant. However, consideration should still be given to this difference as high body fat and low fat free mass are independent predictors of all-cause mortality. With previous studies indicating the
potential for poorer body compositions in this population, maintenance of a healthy body composition should be encouraged for individuals recovering from ACLR.

It is well-understood that elevated BMI throughout the lifespan can have adverse consequences on health, placing individuals at greater risk for noncommunicable diseases such as hypertension, diabetes, heart disease, and premature mortality and morbidity. Recently, a study by MacAlpine et al. determined that pediatric ACLR patients with a normal BMI experienced increases in BMI percentile that persisted up to two years post-surgery. This suggests that ACLR may have detrimental long-term effects on body mass. However, the study did not measure body composition so it is unclear if the mass accumulated during the two years following surgery was primarily fat or muscle. In the current study, 40% (6/15) individuals with ACLR were considered overweight or obese according to BMI (>25 kg/m²), while no uninjured participants had a BMI in these categories. In 2017-2018, the National Center for Health Statistics reported that the prevalence of obesity among adults over age 20 in the US general population was 42.5%, with 73.6% of adults being considered overweight or obese. While the participants with ACLR in this study have a lower prevalence of overweight and obesity classification than the US population, these results are still concerning because previous literature has reported that obesity is a risk factor for reinjury, early ACL revision, and worse patient-reported outcomes at 2 and 6 years after ACLR. Additionally, a BMI >30 kg/m² is a risk factor for osteoarthritis development and progression following ACLR. BMI is a feasible metric to monitor throughout rehabilitation and recovery; therefore, it is recommended that BMI is tracked during this
time and that patients are encouraged to maintain or strive for a BMI that is in a healthy range (18.5 to < 25.0 kg/m²).

Patients with ACLR may experience persistent negative effects on PA engagement such as reduced step counts per day and reduced amounts of time spent in MVPA.¹⁻³ In the current study, daily step counts were similar between groups with our group of individuals with ACLR actually participating in more steps per day as compared to uninjured individuals, although it was not statistically significant. These findings are in conflict with results of previous studies indicating a reduced step count among individuals with ACLR.¹⁻³ Although the majority of participants in both groups spent adequate time in MVPA throughout the week to meet aerobic PA recommendations, few participants in each group achieved recommended step counts of at least 10,000 steps per day.⁵⁸ Only 13% (2/15) participants with ACLR and 13% (1/8) participants without a history of injury had on average over 10,000 steps per day, which is comparable to previous research that found only 24% of individuals with ACLR met step count recommendations.¹ Previously it was found that individuals with ACLR were 2.36x less likely to meet weekly MVPA recommendations.¹ Conversely, participants in both groups for this study showed similar activity patterns with 94% (15/16) of individuals with ACLR achieving at least 150 minutes of MVPA on average for the week, compared to 88% (7/8) of uninjured individuals. This study had a large variance in time since surgery (average 33 months, range 9-66 months) and therefore it seems that the majority of these individuals had successfully returned to activity following ACLR, which may account for the lack of differences in PA engagement. Participants were also matched based on self-reported PA level using the Tegner Activity Scale, which may
also provide another possible reason for the lack of difference in PA engagement. Additionally, many of the participants in this study were recruited from a Kinesiology department on campus and from local recreational sports leagues, which may explain why PA levels were higher than expected in both groups.

Due to the reductions in PA engagement observed in previous studies, we hypothesized that individuals with ACLR may also exhibit lower CRF than their uninjured peers because reduced PA often results in diminished CRF. Similar to previous research in a small sample of women, we did not see a difference in CRF based on our main outcome of interest, relative VO$_{2peak}$ (ml/kg/min). However, participants with a history of ACLR displayed significantly shorter times to exhaustion on the treadmill by almost 2 minutes of exercise time, indicating there may be a difference in CRF if a larger sample size was assessed. Effect sizes indicate also indicate a large effect for injury status on treadmill time to exhaustion. Although it is difficult to make comparisons with an elite athlete population, our results are also in conflict with a study in professional male soccer players that found CRF to be significantly reduced following ACLR. The high volume of MVPA in both groups of this study may provide some explanation as to why no differences in CRF were detected between groups as it is allowing for maintenance of CRF in the ACLR group. Lastly, we did not observe any differences in cfPWV between groups. This finding is not entirely surprising as the sample of participants in this study are young (ages 18-30) and generally healthy. Greater duration of weekly PA is associated with lower arterial stiffness and the participants in this group were highly active which is favorable for arterial stiffness. The standard cut off-value for cfPWV in the prediction of CV events is 10 m/s, the
participants in this study were well below this velocity (ACLR: 6.4 ± 0.8 m/s, uninjured: 6.3 ± 0.8 m/s) indicating they are not at high risk based on this parameter. The cfPWV values obtained in this study are similar to normative values reported in other studies for this age group so ACLR does not seem to affect cfPWV in this sample of participants. It is possible that young patients may experience weight gain and changes in body composition in the short term following ACLR and these changes may not yet be manifesting in negative CV outcomes at this time.

The cross-sectional design of this study limits our ability to make conclusions regarding the causal nature of the relationship between history of ACLR, PA engagement, and the effects on CRF, arterial stiffness, and body composition. Additionally, this study includes preliminary data from a small, highly active sample size of individuals which may not be representative of all individuals with a history of ACLR and thus limits our ability to make generalizations about this population. Despite the attempt to match groups tightly based on age, sex, and Tegner activity level, there was an imbalance of sample size and in sexes between groups with the uninjured control group only having enrolled one male participant. The lack of matching between groups may have impacted our findings, particularly in regard to body composition and CRF results.

CONCLUSION

The findings from this study indicate that individuals with ACLR may experience elevated BMI and fat mass following surgery and end a maximal graded exercise test sooner than their uninjured peers. Overall however, it appears that individuals with a
history of ACLR display similar characteristics of CV health including participation in adequate levels of MVPA per week, similar percent body fat, and comparable CRF and arterial stiffness measurements. Unlike previous investigations we did not find persistent deficits in PA engagement that may result in negative effects on these measurements. The current findings are encouraging that individuals with a history of ACLR are participating in high volumes of PA and are not experiencing deficits in CRF, however, we cannot ignore the potential undesirable changes to weight status in this population. The months and years following ACLR may present a window of opportunity for researchers and clinicians to promote healthy behaviors and these results also demonstrate the need for consideration of PA and diet during clinical care and rehabilitation to ensure that ACLR does not become a risk factor for CVD.
Table 8. Participant demographic information.

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<th>ACLR N = 16</th>
<th>Uninjured n = 8</th>
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<td>Sex (M/F)</td>
<td>6/10</td>
<td>1/7</td>
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<tr>
<td>Age (yrs)</td>
<td>21.8 ± 3.2</td>
<td>22.8 ± 3.5</td>
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<tr>
<td>Height (cm)</td>
<td>168.9 ± 11.6</td>
<td>168.0 ± 4.3</td>
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<tr>
<td>Body Mass (kg)</td>
<td>68.8 ± 12.3</td>
<td>58.8 ± 6.3</td>
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<td>IKDC (0-100)</td>
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<td>98.9 ± 2.0</td>
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<td>Current Tegner Level</td>
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<td>7 [5 to 9]</td>
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<tr>
<td>Time Since Surgery (mo.)</td>
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<td>Meniscus Injury (Yes/No)</td>
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<td>Injury Type (Contact/Non-Contact)</td>
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Values presented as mean±SD unless otherwise indicated. ACLR, anterior cruciate ligament reconstruction; BTB, Bone-tendon-bone, HAS, hamstring autograft. *P<0.05

Table 9. Anthropometric and body composition results.

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<th>ACLR n = 15</th>
<th>Uninjured n = 7</th>
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<th>ηp²</th>
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<td>58.8 ± 6.3</td>
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<td>BMI (kg*m⁻²)</td>
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<td>Body Fat (%)</td>
<td>26.5 ± 8.4</td>
<td>21.5 ± 5.3</td>
<td>0.185</td>
<td>0.09</td>
</tr>
<tr>
<td>Fat Mass (kg)</td>
<td>18.4 ± 6.9</td>
<td>12.3 ± 3.1</td>
<td>0.017*</td>
<td>0.25</td>
</tr>
<tr>
<td>Fat Free Mass (kg)</td>
<td>50.2 ± 10.1</td>
<td>45.0 ± 4.9</td>
<td>0.078</td>
<td>0.15</td>
</tr>
</tbody>
</table>

*P<0.05
Table 10. Device-measured physical activity results.

<table>
<thead>
<tr>
<th></th>
<th>ACLR n = 15</th>
<th>Uninjured n = 8</th>
<th>p-value</th>
<th>η_p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVPA (mins/week)</td>
<td>353.7 ± 181.1</td>
<td>281.6 ± 84.3</td>
<td>0.28</td>
<td>0.06</td>
</tr>
<tr>
<td>MVPA (% time)</td>
<td>6.3 ± 3.1</td>
<td>4.7 ± 1.2</td>
<td>0.16</td>
<td>0.10</td>
</tr>
<tr>
<td>Mean Step Count (steps/day)</td>
<td>8376 ± 3235</td>
<td>7267 ± 2138</td>
<td>0.38</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*p<0.05.

Table 11. Cardiorespiratory fitness and carotid-to-femoral pulse wave velocity results.

<table>
<thead>
<tr>
<th></th>
<th>ACLR n = 16</th>
<th>Uninjured n = 8</th>
<th>p-value</th>
<th>η_p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse Wave Velocity (m/s)</td>
<td>6.4 ± 0.8</td>
<td>6.3 ± 0.8</td>
<td>0.974</td>
<td>0.00</td>
</tr>
<tr>
<td>Time to Exhaustion (min)</td>
<td>21.9 ± 2.5</td>
<td>23.9 ± 1.9</td>
<td>0.038*</td>
<td>0.18</td>
</tr>
<tr>
<td>VO₂peak (L·min⁻¹)</td>
<td>3.0 ± 0.6</td>
<td>2.7 ± 0.4</td>
<td>0.636</td>
<td>0.06</td>
</tr>
<tr>
<td>VO₂peak (ml·kg⁻¹·min⁻¹)</td>
<td>42.8 ± 7.9</td>
<td>45.4 ± 5.2</td>
<td>0.238</td>
<td>0.01</td>
</tr>
<tr>
<td>Maximal Heart Rate (bpm)</td>
<td>189 ± 10</td>
<td>190 ± 9</td>
<td>0.697</td>
<td>0.01</td>
</tr>
<tr>
<td>Lactate Maximum (mmol/L)</td>
<td>10.3 ± 2.6</td>
<td>10.9 ± 3.2</td>
<td>0.697</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*p<0.05
APPENDICIES
APPENDIX A. TEGNER ACTIVITY SCALE

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

BEFORE INJURY:  Level_________  CURRENT:  Level_________

| Level 10 | Competitive sports- soccer, football, rugby (national elite) |
| Level 9  | Competitive sports- soccer, football, rugby (lower divisions), ice hockey, wrestling, gymnastics, basketball |
| Level 8  | Competitive sports- racquetball or bandy, squash or badminton, track and field athletics (jumping, etc.), down-hill skiing |
| Level 7  | Competitive sports- tennis, running, motorcars speedway, handball |
|          | Recreational sports- soccer, football, rugby, bandy, ice hockey, basketball, squash, racquetball, running |
| Level 6  | Recreational sports- tennis and badminton, handball, racquetball, down-hill skiing, jogging at least 5 times per week |
| Level 5  | Work- heavy labor (construction, etc.) |
|          | Competitive sports- cycling, cross-country skiing, |
|          | Recreational sports- jogging on uneven ground at least twice weekly |
| Level 4  | Work- moderately heavy labor (e.g. truck driving, etc.) |
| Level 3  | Work- light labor (nursing, etc.) |
| Level 2  | Work- light labor |
|          | Walking on uneven ground possible, but impossible to back pack or hike |
| Level 1  | Work- sedentary (secretarial, etc.) |
| Level 0  | Sick leave or disability pension because of knee problems |

APPENDIX B. THE MARX ACTIVITY SCALE

MARX SCALE (ENGLISH VERSION)

Please indicate how often you performed each activity in your healthiest and most active state, in the past year. Kindly put a (☑) mark on the appropriate space after each item.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Less than one time in a month</th>
<th>One time in a month</th>
<th>One time in a week</th>
<th>2 or 3 times in a week</th>
<th>4 or more times in a week</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Running:</strong> running while playing a sport or jogging</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Cutting:</strong> changing directions while running</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Deceleration:</strong> coming to a quick stop while running</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Pivoting:</strong> turning your body with your foot planted while playing sport; For example: skiing, skating, kicking, throwing, hitting a ball (golf, tennis, squash), etc.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
APPENDIX C. THE INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE – SHORT FORM (IPAQ-SF)

1a. During the last 7 days, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?
   Think about only those physical activities that you did for at least 10 minutes at a time.
   _______ days per week ⇒ 1b. How much time in total did you usually spend on one of those days doing vigorous physical activities?
   or
   ■ none
   _______ hours _______ minutes

2a. Again, think only about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.
   _______ days per week ⇒ 2b. How much time in total did you usually spend on one of those days doing moderate physical activities?
   or
   ■ none
   _______ hours _______ minutes

3a. During the last 7 days, on how many days did you **walk** for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure.
   _______ days per week ⇒ 3b. How much time in total did you usually spend walking on one of those days?
   or
   ■ none
   _______ hours _______ minutes

The last question is about the time you spent **sitting** on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.

4. During the last 7 days, how much time in total did you usually spend sitting on a week day?
   _______ hours _______ minutes

This is the end of questionnaire, thank you for participating.

This is the final **SHORT LAST 7 DAYS SELF-ADMINISTERED** version of IPAQ from the 2000-01 Reliability and Validity Study. Completed May 2001.
BACK MATTER – RECOMMENDATIONS FOR FUTURE RESEARCH

While this dissertation work addressed some of the gaps in the current literature, more studies need to be conducted to further assess the relationships between ACLR, PA, and long-term CV health outcomes in this population. Future research should include longitudinal studies to assess the patterns of PA, changes in BMI and body composition, and CRF in the months and years following ACLR. Finally, interdisciplinary work that involves orthopedic surgeons, primary care physicians, physical therapists, and researchers is needed in order to develop clear communication pathways for evaluating and optimizing rehabilitation protocols to include PA promotion and encouragement of healthy lifestyle behaviors for patients with ACLR.
REFERENCES


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64. Briggs KK, Lysholm J, Tegner Y, Rodkey WG, Kocher MS, Steadman JR. The Reliability, Validity, and Responsiveness of the Lysholm Score and Tegner Activity


