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Associations of Cardiovascular Health, Strength, and Physical Activity in Participants with a History of Anterior Cruciate Ligament Reconstruction

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Associations of Cardiovascular Health, Strength, and Physical Activity in Participants with a History of Anterior Cruciate Ligament Reconstruction

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I. Review of the Literature

1.1 Anterior Cruciate Ligament Injury, Reconstruction, and Rehabilitation

1.11 Prevalence

Anterior cruciate ligament (ACL) tears are among some of the most studied orthopedic injuries in sports medicine. Although a true incidence of ACL injury in the United States is unknown, it is estimated that approximately 200,000 ACL injuries occur annually, with 100,000 to 150,000 of these undergoing reconstructive surgery.[1] Notably, the infusion of more young individuals participating in high level sports and more older adults being physically active later into their lives has led to greater number of ACL injuries in the recent years.[1] High school athlete knee injuries account for 60% of sport-related surgeries, and some studies report that ACL injuries are responsible for 50% of these knee surgeries.[2] Unfortunately, 20-25% of individuals with a history of ACL injury will experience a secondary knee injury event that requires further management.[3] With ACL injuries being reported as costing the US health care system an estimated $7.6 billion dollars annually, this common musculoskeletal injury is a major economic burden.[4]

1.12 Injury

ACL injuries have two primary mechanisms, contact and non-contact. Non-contact mechanisms of injury account for up to 70% of all ACL injuries, and most commonly occur while cutting or single legged landing.[5] Individuals most commonly report feeling or hearing a pop, or feeling their knee giving way.[2]

1.13 Surgical Reconstruction

ACL reconstructive techniques most commonly include autografts and allografts. Autografts consist of harvesting the individual's hamstring tendon or patellar tendon. The patellar tendon, most commonly called the bone-patellar tendon-bone technique, has been considered the gold-standard for ACL reconstruction (ACLR), but both techniques (hamstring and patellar tendon) are commonly used, and both have equivalent results when considering graft failure following surgery.[6] Although, when comparing allograft and autograft options, Kaeding et al 2010 found that individuals with allografts were 4 times more likely to experience a subsequent rupture.[7]

1.14 Known Complications with ACLR

Following ACLR, most individuals participate in a 6-9-month rehabilitation program. The goal of these rehabilitation programs is to generally increase strength and decrease pain by utilizing a combination of therapeutic exercises that drive to improve functional movements and neuromuscular control, self-efficacy, and kinesiophobia.[8] Though the surgical repair of the ACL successfully reestablishes static stability of the knee, dynamic stability of the knee, which is directly impacted by quadricep muscle strength[9], is not often regained.[10,11]

Two major factors that influence strength recovery following ACL injury are quadricep activation failure and atrophy.[12] Quadricep activation failure is commonly experienced following ACLR and is identified when and individual is unable to volitionally contract the entire quadricep muscle due to changes in their neural activity;

whereas atrophy occurs as a result to of the loss of muscle volume. Together, these factors have been found to account for up to 60% of the variance of quadricep muscle strength following ACLR.[13] Quadricep strength influences range of motion, functional movements, and stability and control; showing how vital it is to target this factor during rehabilitation. Although most rehabilitation plans are extensive and complex, it is reported that reestablishing their knee to pre-injury status seldomly occurs.[8] If an individual has not regained full, or close to full, quad strength this could put them at higher risk for reinjury and therefore should not return to full activity.[10]

Patient reported outcome measures (PROM) can also provide valuable information when examining a patient and their status during rehabilitation. Following traumatic knee injury, a means to identify the changes in symptoms and function over time that covers both the short and long term is essential.[14] Utilizing these outcome tools can provide un-bias information on how a patient is feeling about their knee, how confident they are, their pain levels, and even how they believe they are doing in the rehabilitation process.

1.15 Re-injury

Re-injury rates are a growing interest and issue when considering ACLR, rehabilitation, and return to play. In a systematic review and meta-analysis completed by Wiggins et al in 2016, it was found that the overall ACL reinjury rate was 15% (7% for ipsilateral and 8% for contralateral limbs). Additionally, for patients under the age of 25 years old, the re-injury rate increased to 21%.[15] This is nearly 1 in 4 individuals that will experience a second catastrophic injury to their knee. This statistic suggests that further considerations need to be taken when designing rehabilitation protocols and return to play guidelines.

It is also important to consider the long-term effects that a second ACL injury can have on the body. A single ACL rupture can cause quadricep strength deficits, early onset osteoarthritis, and a reduced quality of life.[16] Suffering from a second ACL injury accelerates this timeline and exacerbates the significant comorbidities experienced by those with a singular ACLR.[17]

1.2 Deconditioning and Cardiovascular Health

1.21 Deconditioning

An underappreciated consequence of ACL injury that is gaining attention in the literature are cardiovascular health complications. Following surgical reconstruction, ACLR individuals experience a necessary phase of reduced physical activity and deconditioning to protect the healing graft. During this initial phase, individuals are striving to control swelling and pain, reestablish neuromuscular control and range of motion, and to be ambulating without assistance.[18,19] Aerobic exercise is generally contraindicated due to lack of strength, control, stability, and risk of compromising the graft. During this period of inactivity, the patient's cardiovascular system experiences a phase of deconditioning resulting in a decrease in work capacity. Reductions in work capacity metabolically lead to decreased left and right ventricular volumes and total heart volume. To this point, early data by Steding-Ehrenborg et al 2013 discovered that resting heart rate (HR) and total heart volume were significantly affected by the early acute period of inactivity in individuals following ACLR.[20] This phase of deconditioning that occurs post-ACLR therefore stands to negatively affect the cardiovascular system.

Given the high rate of re-injury, it is also important to consider the effects that ACL re-injury can have on the cardiovascular system. In this turn of events, an individual experiences not one, but two (or more), phases of deconditioning. Additionally, concurrent ACL injuries have been shown to compound the issues of quadricep inhibition, accelerated onset of osteoarthritis, and a reported lower quality of life.[17] All of these factors influence one's ability to participate in physical activity, and therefore have the potential to further exacerbate the health of their cardiovascular system. Sparse data is available that points to the negative effects of a single ACLR on the cardiovascular system.[21,22] The effect of multiple injuries have yet to be uncovered, though it stands that multiple periods of deconditioning would likely negatively impact cardiovascular health.

1.22 Protracted Cardiovascular Impairments After Anterior Cruciate Ligament Injury: A Critically Appraised Topic – See Appendix A

1.3 Examining Cardiovascular Health

1.31 Heart Rate, Heart Rate Recovery, and Blood Pressure

Simple, non-invasive measures of cardiac health are imperative to assessing where a patient's condition lies. Examining HR, blood pressure (BP), and heart rate variability (HRV) are simple, reasonable measures to take advantage of during rehabilitation that can provide meaningful markers of cardiovascular health.

HR's response to exercise and the subsequent recovery phase can offer unique information into the efficiency of an individual's cardiovascular system.[23,24] Briefly, during exercise, the cardiovascular system works to respond to external stressors. This causes a stimulation of the sympathetic nervous system, that in turn, leads to a dilation of blood vessels in the active muscles, and a decrease in vagal outflow to the heart. As exercise intensity increases, a release of epinephrine into the circulatory system, increases venous return, contractility, and HR. Additionally, ejection fraction increases causing an increase in HR and BP in order to supply the systems under pressure with oxygen and nutrients.[23] When these mechanisms do not fire or work together properly, it is called chronotropic incompetence.

Chronotropic incompetence and HR's response to a recovery period have been associated with mortality and sudden cardiac death.[23,24,25] Although the true cause of chronotropic incompetence is unknown, it is speculated that it is related to the desensitization of efferent nerves that effect the sinoatrial node. All of this is in response to persistent overfiring of the SNS pathways.[26]

Overall, during physical activity, the sympathetic nervous system is responsible for causing physiological adaptations. When the body moves from a resting state to a physically active state, there is a decrease in vagal tone (or parasympathetic output) followed by an increase in sympathetic activity. All of these immediate adaptations allow the body to provide adequate nutrients and energy to the structures being stressed.

Following a bout of physical activity, the body must return to its resting state, deemed heart rate recovery (HRR). This is described as increased parasympathetic tone succeeded by sympathetic withdrawal[23,27], and is defined as the period of time immediately following exercise in which HR declines, working back down towards its resting value.[27]

Healthy individuals exhibit low resting HR and quick HRR following exercise. Conversely, a high resting HR and slow HRR are indicative of cardiovascular disease. Physical activity is currently prescribed to combat against cardiovascular disease and high blood pressure. It has also been shown that physical activity causes lower resting HR and improves HRR.[28] Modern society is becoming more habitual with sedentary activities, and consequently causing an increase in chronic diseases such as cardiovascular disease and cardio chronic obstructive pulmonary disease. With patients recovering from ACL already starting behind the curve with impacted cardiovascular systems, it is important to motivate them during and after rehabilitation to participate in exercise regularly.

1.32 Heart Rate Variability

HR is defined as the number of beats per minute, whereas heart rate variability is described as the fluctuation of time in between each consecutive beat.[29] Heart rate is controlled by the autonomic nervous system (ANS), and the ANS is broken up into two branches: the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). The ANS controls the body's involuntary functions, including HR, gastrointestinal tract, respiration, and many gland secretions.[30] The sinus node of the heart, the location where the heartbeat is initially stimulated, is innervated by both the SNS and PNS. The SNS is responsible for regulating stresses on the body and accelerates

HR, whereas the PNS is responsible for slowing HR and returning the body to its resting state.[31]

The heart is not a metronome that experiences evenly spaced beats over time. Shaffer et al 2017 describes the oscillations of the heart as being complex and non-linear, and the fluctuations between each heartbeat as mathematical chaos.[29] Each individual heartbeat is dependent on both the SNS and ANS, and how each of these systems respond to whichever state the body is in, rest or activity.[32] Exercise causes an increase in SNS activity and is accompanied with PNS withdrawal, allowing for the cardiovascular system to become more active and address physical stressors[33], and the opposite occurs when the body is transitioning back to rest.

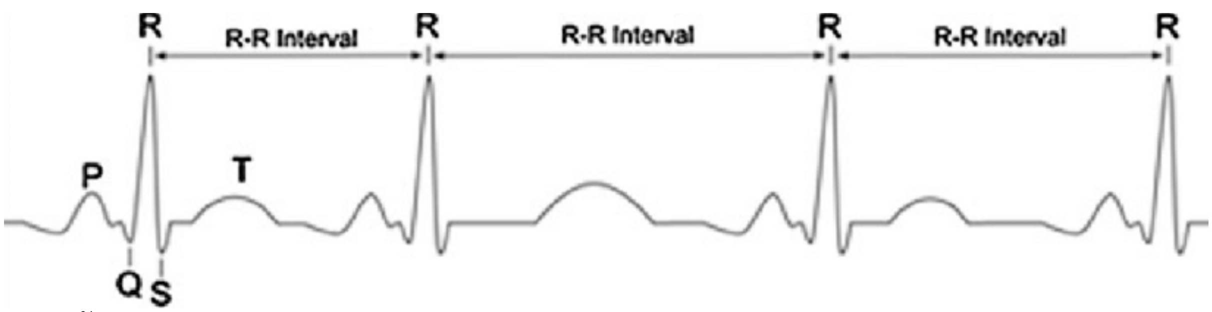

Image 1.[34]

When analyzing HRV, the time is plotted between each R wave, called an R-R interval. The time that passes between each beat is then calculated and analyzed. When an individual experiences low variability, this is usually due to an overactive SNS and underactive PNS. This state explains that the body is unable to adapt and respond to external stressors, such as exercise.[30] This could be indicative of hypertension, cardiovascular disease, mortality, and many more chronic conditions.

Following ACLR, HRV can be a very beneficial tool in examining the cardiovascular system. To date, there is little to no research on the relationship between ACLR and HRV trends. HRV research is continuing to show how useful and beneficial results can be and is an easy outcome to refer to during ACL rehabilitation protocols. As stated above, the phase of deconditioning that individuals experience following ACLR can potentially have debilitating effects on the cardiovascular system, but further research is needed to determine the extent of deconditioning and possible pathology.

1.4 Patient Reported Physical Activity and ACL Injury

1.41 Patient Reported Outcome Measures (PROM)

A patient reported outcome measure is qualitative measure completed by the patient that describes the status of their treatment, healing, health, quality of life, or functionality without any influence from a clinician or anyone else.[35,36] These tools are efficient, non-invasive, techniques that provide clinicians with direct input from their patients of their status from different domains. PROM also give patients an opportunity to have a method to describe their symptoms on paper. This perspective that is provided by the patient provides the medical provider with a more holistic interpretation and comprehensive evaluation of the care being provided.[35]

Following ACLR, the goals of rehabilitation programs include increasing strength, decreasing pain, improving neuromuscular control, and ultimately returning to sport.[8] Although, these goals can be affected due to delays in physical therapy, self-efficacy, and kinesiophobia. PROMs provide patients with a subjective method to communicate their physical symptoms, mindset, physical activity, and more.

Following traumatic knee injury, a means to identify the changes in symptoms and function over time that covers both the short and long term is essential.[14] Pain can be one of the hardest symptoms for patients to describe to their physicians, and therefore hinders their activities of daily living and participation in physical activity.

1.42 Patient Reported Activity Levels and ACLR

Part of PROMs is patient reported activity levels. As previously mentioned, participation in physical activity following ACLR is a major factor to be addressed during rehabilitation and afterwards. Many individuals suffering from chronic disease experience decreased activity levels due to the exacerbation of symptoms during movement. Although, this draws concern considering the common subscription of physical activity to combat chronic disease.[36] Patient reported outcome measures allow individuals to quantify and share with their practitioner current activity levels. Utilizing PROMs, like the Tegner activity scale, can provide clinicians with valuable information on their patient's current quality of life and how it could be influencing their recovery.

The Tegner Physical Activity Scale is used to quantify physical activity levels prior to and after reconstruction and the succeeding rehabilitation.[36] This scale consists of levels 0 through 10. The bottom of the scale, 0, represents no physical activity and not being able to work due to pain or knee related problems. The top of the scale, 10, signifies competitive sports at an elite level.

1.5 Clinical Implications

In recent studies, it has been shown that individuals following ACLR have a lower daily step count, spend less time in moderate to vigorous physical activity, experience decreased maximal oxygen consumption, and have a >50% chance of myocardial infarction.[16,21,22,37] These preliminary studies provide a gateway into another realm of ACL research. Although the cardiovascular system following ACLR may not experience noticeable, acute, changes, it is an important factor to address in order to ensure a high quality of life. During ACL rehabilitation, including endurance and cardiovascular training along with pain management and strength training will be beneficial; and using measures such as HR, HRR, and HRV provide easy, noninvasive techniques that provide simple data to analyze and have real time information on the status of one's cardiovascular system.

Additionally, utilizing self-reported physical activity provide beneficial information to clinicians regarding the knee status and how it effects patients' daily lives. These tools can provide insight into a variety of patient domains, including: current pain levels, how it effects their physical activity, how often they are participating in physical activity, and even how confident they are while participating. Physical activity is vital in preventing chronic disease like cardiovascular disease and chronic obstructive pulmonary disease. Being able to address declines in physical activity post-ACLR acutely could be essential in preventing chronic diseases, and PROMs make this quick and easy.

The results of this study start to close the gap between the lack of knowledge of cardiovascular health and ACLR becomes smaller. Most studies that have been addressed in this literature review deal with direct cardiovascular outcomes (VO2max, ventilatory thresholds, stroke volume, etc.) and focus on a short-term timeline [21,22]; whereas this study focused more on individuals that are further out from reconstruction (>2 years) and have multiple ACL injuries. The ultimate goal of this study is to provide information to clinicians on the potential implications of multiple knee joint injuries to cardiovascular health and the importance of shifting the focus of ACLR rehabilitation away from simply strength training to including cardiovascular training during the rehabilitation process.

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1.7 Appendix A

Protracted Cardiovascular Impairments After Anterior Cruciate Ligament Injury: A Critically Appraised Topic

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Journal of Sport Rehabilitation

ABSTRACT

Clinical Scenario: Anterior cruciate ligament (ACL) tear is a devastating knee injury with negative long-term consequences, such as early-onset knee osteoarthritis, biomechanical compensations, and reduced physical activity. Significant reduction in physical activity is a powerful indicator of cardiovascular (CV) disease, hence those with a history of ACL injury may be at increased risk for CV disease compared to non-injured individuals. ***Focused Clinical Question:*** Do individuals with a history of ACL injury demonstrate negative CV changes compared to those without a history of ACL injury? ***Summary of Key Findings:*** Three articles met the inclusion criteria and investigated CV changes after ACL injury. Both cross-sectional studies compared ACL injury participants with matched controls. One study[1] compared time spent in moderate to vigorous physical activity (MVPA) and step count. The other investigation[2] compared maximum rate of oxygen consumption (VO2max), ventilatory thresholds, isokinetic quadriceps strength, and body composition. Collectively, both quantitative studies found that individuals with a history of ACL injury had less efficient CV systems compared to matched controls and/or pre-operative data. Finally, a qualitative study[3] of 3,506 retired National Football League (NFL) athletes showed an increased rate of arthritis and knee replacement surgery after an ACL injury when compared to other retired NFL members, in addition to >50% increased

rate of myocardial infarction. ***Clinical Bottom Line:*** A history of ACL injury is a source of impaired physical activity. Preliminary data indicate these physical activity limitations negatively impair the CV system, and individuals with a history of ACL injury demonstrate lower maximum oxygen consumption, self-reported disability and daily step count compared to non-injured peers. These complications support the need for greater emphasis on CV wellness. ***Strength of Recommendation:*** Consistent findings from two cross-sectional studies and one survey study suggest level IIB evidence to support that ACL injury is associated with negative CV health.

CLINICAL SCENARIO: Traumatic knee injuries leads to a multitude of negative effects on the body, including altered physical activity, biomechanical compensations and early onset knee osteoarthritis.[3,4,5] Individuals recovering from anterior cruciate ligament ACL injury spend less time in MVPA, and take fewer steps per day compared to healthy individuals.[1] Significant reductions in physical activity are a powerful indicator of cardiovascular disease. Accordingly, those with a history of ACL injury may be at an increased risk of cardiovascular disease compared to their non-surgical peers.

FOCUSED CLINICAL QUESTION: Do individuals with a history of an ACL injury demonstrate negative cardiovascular changes as compared to those who have not experienced an ACL injury?

SUMMARY of Search, 'Best Evidence' appraised, and Key Findings:

- A literature search was performed to investigate cardiovascular changes after ACL injury.

- All studies must have investigated the protracted cardiovascular changes (such as heart rate, blood pressure, oxygen consumption) following ACL injury.
- Of the initial 106 articles retrieved, 3 met the inclusion criteria: 2 cross sectional studies, and 1 qualitative survey.
- Cardiovascular testing ranged from pre-surgery to 6 months post-surgery[2] as well as multiple years post-surgery.[1]
- Both cross-sectional studies[1,2] compared ACLR participants with matched healthy controls. One study used accelerometers and measured time spent in MVPA and step count between groups (ACLR v. controls) for seven days. The other cross-sectional investigation compared maximum rate of oxygen consumption (VO2 max), ventilatory thresholds, isokinetic strength, and body composition between groups. It examined ACL injured participants at pre-surgery and 6 months post-operation. Results were also compared to healthy controls.
- The qualitative survey study[3] showed an increased rate of arthritis and knee replacement surgery after an ACL injury. In addition, although statistical significance was not reached, there was >50% increased rate of myocardial infarction in players with a history of ACL tear.
- Although one study found that participants with a history of ACL injury had better cardiovascular outcomes compared to pre-surgical data,[2] collectively, both cross sectional studies found that individuals with a history of ACL injury had less efficient cardiovascular systems compared to healthy controls.
- Deficits in oxygen consumption, heart rate and self-reported function associated with cardiac events were observed in the ACL injured groups.

CLINICAL BOTTOM LINE: A history of an ACL injury and reconstruction significantly influences physical activity. For instance, those with a history of ACL injury reportedly have a lower daily step count and decreased aerobic fitness.[1] These significant declines in physical activity may negatively impair the cardiovascular system. Strikingly, a recent qualitative report concluded that those with a history of ACLR reportedly have an >50% increased risk of myocardial infarction.[3] This risk of cardiovascular disease, alongside the well-established risk early onset osteoarthritis complications that plague this population, may indicate that individuals with a history of ACL injury that develop early onset osteoarthritis are at an increased risk of cardiovascular disease.[3] Though these are early data, this link between osteoarthritis and cardiovascular disease has been found in idiopathic osteoarthritis development.[6,7] Altogether, this clinical scenario suggests that there is a risk of cardiovascular complications after ACL injury and there is a need to consider incorporating cardiovascular-focused rehabilitation strategies. **Strength of Recommendation:** Consistent preliminary findings from two cross-sectional studies and one survey study suggest level IIB evidence to support that ACL injury is associated with negative cardiovascular health.

Search Strategy

Terms used to guide search strategy:

- Participant/Client Group: Individuals who have undergone knee surgery
- Intervention/Assessment: Cardiovascular function (VO2max, BP, HR, HRV, cardiovascular disease)
- Comparison: Non-surgical

- Outcome: Aerobic fitness or cardiovascular function/disease

Sources of Evidence Searched (databases)

- Pubmed
- Sportsdiscus

INCLUSION AND EXCLUSION CRITERIA

Inclusion:

- Human participants only
- Articles available in English language
- Group of post-knee orthopedic surgical participants
- Measure of cardiovascular health (VO2max, BP, HR, HRV, cardiovascular disease)

Exclusion:

- Animal participants
- Languages other than English
- Participants with other major lower extremity injury

Results of Search

Three relevant studies were located and categorized as shown in Table 1.

Table 1: Summary of Study Design of Articles Retrieved

The following studies were identified as the 'best' evidence and selected for inclusion in the CAT. Reasons for selecting these studies were:

- All studies matched the inclusion/exclusion criteria.
- All studies contain groups with a knee specific orthopedic surgery.
- All studies utilized cardiovascular based outcomes.

Table 2: Summary of Best Evidence

Implications for Practice, Education, and Future Research

The two cross-sectional studies included in this critically appraised topic found a significant decrease in cardiovascular measures when compared to healthy controls.[1,2] Both studies compared the results of athletes (ages 20 - 22 years old) that had torn their ACL and underwent reconstructive surgery versus a healthy-matched control. Bell et al.[1] found that individuals with a history of ACL injury spent less time in MVPA and had lower daily step counts, which are variables that have a direct effect on cardiovascular health. Marques de Almieda et al.[2] evaluated the cardiovascular system via VO2 max and ventilatory thresholds, as well as a knee function questionnaire, isokinetic strength test, and body composition measurement. This study found that participants with a history of ACL injury scored significantly lower in all categories. Cumulatively, these results indicate those with a history of ACL injury may be at risk for a compromised cardiovascular system compared to their non-surgical peers.[1,2] Finally, the qualitative study showed that out of 3,506 former NFL athletes, those that had torn their ACL had a higher incidence of myocardial infarction as compared to other retired NFL members.[3] In summary, there is a short-term, immediate problem demonstrated by the two cross-sectional studies reporting significant reductions in physical activity; and long-term, there is a troubling qualitative study that points to a high incidence of cardiac events.

On a global scale, ACL ruptures occur in 300,000 Americans every year,[8] with a reported re-injury rate as high as 23%,[9] which may also influence declines in physical activity rates. These statistics, in conjunction with the findings of this critically appraised topic, and the link between osteoarthritis and cardiovascular disease in idiopathic populations,[6,7] demonstrate the necessity of further studies to better determine the long-term impairments of ACL injury.

Although there is extensive literature studying the long-term changes of ACL injury on the knee joint,[10] the evidence regarding the long-term cardiovascular changes after knee surgery is limited, and as such, future research is needed to better understand the early signs of cardiovascular distress and how it evolves over time. A refined understanding of the timeline of cardiovascular changes would help both the researcher and clinician better understand how to treat these impairments transcribed from ACL injury. It is important to note, that of the three appraised articles, only one assessed cardiovascular fitness pre-surgery.[1] Future research should focus on the effects of ACL injury compared to ACL reconstruction.

Current trends of ACL rehabilitation focus on regaining strength and functional movements for return to play goals. Clinicians tend to tailor therapy to patient-centered goals, such as being able to run, play a particular sport, or successfully perform activities of daily living. Unfortunately, 88% of patients expect to return to sport[11] despite alarmingly high re-injury rates.[9] Plausibly this decline in pre-injury level of sport, could be an important link to cardiovascular disease later in life. Future research will need to evaluate this relationship. The results from this topic indicate a need for greater focus on cardiovascular-based therapy during rehabilitation and encouragement to return to endurance-based physical activity post-rehab. The evidence presented should also encourage clinicians to modify current trends of ACL rehabilitation strategies to also focus on cardiovascular health after ACL injury.

Since the data to observe progressive cardiovascular changes are not yet available, longitudinal studies will be beneficial to understand the relationship between ACL injury and long-tern cardiovascular health. The emerging picture at the very least suggests that cardiovascular fitness should be an important component of rehabilitation that should be on a clinician’s radar.

Acknowledgments

N/A

Conflicts of Interest: There are no conflicts of interest.

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II. Manuscript

2.1 Introduction

Anterior cruciate ligament (ACL) tears are amongst some of the most studied orthopedic injuries in sports medicine, with approximately 200,000 injuries occurring annually and 100,000 to 150,000 of patients electing to have surgical reconstruction in the U.S.[1] In the primary weeks of ACL rehabilitation, weight-bearing aerobic exercises are often limited to protect the healing graft. This restriction leads to exercise programs that generally encompass low-impact, strength building activities in an effort to restore neuromuscular function so that more dynamic, high-impact activities can be added on in the later stages of rehabilitation.[2] However, this significant early period of low impact/ aerobic activity has the potential to lead to whole athlete deconditioning, and thus cardiovascular impairments.[3,4] This period of inactivity may affect an individual's long-term cardiovascular prognosis if not appropriately addressed in the later stages of rehabilitation.

Individuals that recover from their primary ACL injury and reconstruction have been reported to have a 15-30% chance of experiencing a secondary ACL rupture.[5,6] Individuals that sustain a secondary knee injury event may experience greater cardiovascular impairments on the basis that this second traumatic knee injury events lead to longer periods of inactivity. Additionally, these individuals are known to suffer from an earlier onset of osteoarthritis, more muscle weakness, and reduced physical activity levels.[7] Therefore, individuals with multiple ACL reconstructions (ACLR) may have even more compromised cardiovascular systems.

Emerging data suggest a hazardous link between ACL injury and cardiovascular health.[3,8,9] A recent retrospective study of more than 3,500 former National Football

League athletes observed a greater than 50% increased risk of myocardial infarction in athletes with a history of an ACL injury.[9] Furthermore, investigators have found that individuals with a history of ACLR spend less time in moderate to vigorous physical activity.[7] Though the preliminary causal links between ACLR and subsequent cardiovascular health impairments are beginning to emerge, studies that more directly investigate the relationships between ACL injury, cardiovascular health, and physical activity level are missing.

In a preliminary effort to more clearly understand the extent of this problem, the purpose of this study was to identify long-term changes in the cardiovascular health of individuals post ACLR, and in those with a history of multiple ACL injuries. Our hypothesis was that a history of multiple ACL injuries would lead to a less efficient cardiovascular system than those with a single ACLR. Also, we hypothesized that level of recovery (assessed via muscle strength) and physical activity level would be related to cardiovascular health. The results of this study intend to guide clinicians in adjusting their focus from strength driven rehabilitation trends; and given the emerging evidence, expanding that focus to address cardiovascular factors.

2.2 Methods

2.21 Participants

Participants were recruited to take part in this study by word of mouth, social media, posters, and email. The University of Connecticut daily forum was utilized to reach students on campus, as well as word of mouth and referring volunteers to the Sport Optimization and Rehabilitation lab. To be included in this cross-sectional study, all participants were required to be between 18 and 35 years old, to have torn their ACL, and to have self-reported physician clearance to participate in full physical activity following their rehabilitation. Participants with two ACL injuries were included in this study in order to provide insight on the further complications experienced following more than one traumatic knee injuries. Participants were excluded for the following criteria: resting systolic BP was above 200 mmHg; previous history of knee surgery other than ACLR; previous ipsilateral lower extremity injury within the last 6 months; any contralateral lower extremity injury that required surgery within the past 6 months; any type of cardiac pacemaker; any current cardiopulmonary illness (e.g., bronchitis); family history of cardiac disease or sudden unexplained death before age 50; and an inability to participate in physical activity (e.g., running and strength training) due to pain or not having physician clearance. All participants provided written, informed consent prior to the start of the study. The Institutional Review Board at the University of Connecticut approved all procedures of this study.

2.22 Protocol

This cross-sectional study required a single test session. The general format of the testing session included a pre-exercise period, strength testing, an exercise period, and then a post-exercise period. The main outcome variables collected included heart rate (HR), heart rate variability (HRV), and blood pressure (BP), quadricep strength, and self-reported physical activity.

2.23 Instrumentation and Pre-Exercise

To monitor cardiovascular metrics, prior to exercise, each participant was fitted with the Polar TeamPro (Polar Team Pro, Polar Electro, Lake Success, NY). The wearable heart rate monitor was placed, via an elastic strap, around the torso and anterior to the xyphoid process. The device wirelessly connected to an iPad (Apple, 5th Generation, MP2J2LL/A), which was used to capture HR and HRV via the Polar TeamPro application. The TeamPro was worn for the entirety of the participant's trial. After being fitted with the heart rate monitor, participants rested in a supine position for a 10-minute period and were asked to focus on controlled breathing.[10,11] At the end of this 10-minute resting period, resting values for HR, HRV, and BP were collected. Their BP was collected via a manual cuff from their non-dominant arm for consistency and the finding that there are small to no changes in BP between arms.[12]

HRV is defined as the variability of time between each heartbeat and is used to examine cardiovascular regulation.[13] HRV data was extracted from the Polar TeamPro via the Polar website and imputed into Kubios HRV (The Biomedical Signals Analysis and Medical Imaging Group, University of Kuopio, Finland), a data analysis software that corrects artifacts and provides analyzable data. Kubios provides many analyzable HRV data, but for this investigation it provided one statistic in particular called the standard deviation of normal R-R intervals (SDNN), which is a time domain measure of heart rate variability. SDNN analyzes the amount of time between consecutive heart beats and quantifies the amount of parasympathetic (PNS) and sympathetic (SNS) nervous system influence on the cardiovascular system.[14] The consistent interplay of these two systems is crucial for proper homeostasis, one responsible for addressing stress (SNS) and one for calming the body down (PNS).[14,15] A higher SDNN is physiologically representative of a cardiovascular system that allows for greater variability of the autonomic nervous system, which leads to more efficiency during rest, physical activity, and recovery. Conversely, a lower SDNN value is a marker of cardiovascular disease and other comorbidities.

2.24 Patient Reported Physical Activity Levels

After the period of rest, participants were asked to fill out a patient-reported physical activity scale, the Tegner Activity Level Scale. This scale was utilized to quantify physical activity habits. The Tegner is used to report physical activity levels prior to and after returning to play following ACLR.[15] The scale consists of levels 0 to 10, 0 being sick leave from work due to knee pain or problems, and 10 representing competitive sports at a national, elite level.

2.25 Isometric Quadricep Strength

Prior to engaging in exercise, isometric quadricep strength was analyzed using an isokinetic dynamometer (Biodex System 4, Biodex Medical Systems, Shirley NY). The participant was asked to perform a series of 3 maximum voluntary isometric contractions (MVICs) at 90° of knee flexion. The maximum force among these 3 attempts was normalized by body weight and utilized to represent the peak quadricep strength of each participant. This procedure was repeated bilaterally.[16]

2.26 Exercise

All participants then completed an incremental treadmill run on a motorized treadmill (TRM 835 Treadmill, Precor, Woodinville, WA, USA), starting with a comfortable, self-selected jog pace and increasing the speed by 0.5-1.0 mph every 2 minutes. At each 2-minute interval of this test, HR and HRV were measured and recorded.[17] The test was terminated when the participant could no longer maintain the running speed, or when they asked to end due to fatigue, major discomfort/pain, and/or shortness of breath.

2.27 Post-Exercise

Following completion of the exercise portion of the protocol, each participant was asked to lie on his/her back while focusing on controlled breathing. HR, HRV, and BP were then recorded every 2-minutes for a period of 10 minutes. At the conclusion of the final rest period, the HR monitor was removed, and the participant was allowed to leave the lab.

2.3 Statistical Analyses

Pairwise Pearson Correlations were used to evaluate the associations ($p \leq 0.05$) between MVIC, post exercise SDNN, and the Tegner Physical Activity Scale. MVIC was normalized by body weight to account for different body types sizes. Independent t-tests were also used to compare ($p \leq 0.05$) the single ACLR and multiple ACLR groups for all outcome measures, as well.

2.4 Results

The final ACL cohort consisted of 14 individuals, 9 females and 4 males, with demographics of the group described in Table 1. Post-exercise HRV, or SDNN, was found to be positively correlated with the MVIC of the ACL limb (R=0.599, p=0.040, Figure 1). Additionally, following statistical analysis it was found that the Tegner Physical Activity Scale was positively correlated with the MVIC of the affected limb as well (R=0.751, p=0.003, Figure 2).

In a sub-analysis of the single ACLR group to those with multiple ACLRs, it was found that those with a single injury in their lifetime generally had greater quadriceps strength and possessed better HRV values. These results were not statistically significant, but they do provide clinical significance and information for when dealing with individuals suffering from multiple ACLRs (Table 2). Cohens d effect sizes reinforce this observation as both strength and HRV metrics between groups were separated by more than 1 standard deviation (MVIC Cohen's d = 1.00, 95% CI (-0.41, 2.27) and SDNN Cohen's d = 1.07, 95% CI (-0.24, 2.23)).

2.5 Discussion

The purpose of this study was to identify long-term changes in the cardiovascular health of individuals post ACLR, including those individuals that have torn their ACL more than once. This investigation utilized HRV, quadriceps strength, and patient-reported activity levels in order to determine the possible trends and compromises in cardiovascular health after ACLR. This investigation discovered there was a significant positive correlation between cardiovascular health and maximum quadricep strength of the affected limb (R=0.599, p=0.040), along with a significant positive correlation between the Tegner physical activity scale and maximum quadricep strength of the affected limb (R=0.751, p=0.003). When comparing the single ACLR individuals with those with multiple ACLRs, MVIC of the affected limb and cardiovascular measures of the multiple ACLR group were found to be more impaired, though these were not statistically significant (Table 3).

The current findings support the observation that ACL injuries have profound effects on the entire body, and these effects are not confined just within the knee. These traumatic injuries not only cause an early onset of osteoarthritis and decreased muscle strength, but also are associated with a less capable cardiovascular system.[3,8] The inevitable phase of deconditioning during the low-intensity initial phases of rehabilitation may have renowned protracted effects on the rest of the body.[18] Long-term this phase of deconditioning may open the door to other comorbidities.

The investigation of this ACLR cohort showed that increased quadriceps isometric strength was associated with increased heart rate variability, post-exercise (SDNN). This finding illustrates that individuals with higher quadriceps strength have more efficient cardiovascular systems, that recover quicker following a bout of physical activity. During the initial days and weeks following ACLR, quadriceps strength is significantly diminished; and recovering from this strength deficit is an imperative part of long-term ACL rehabilitation and a factor in the return to activity decision. Encouraging consistent physical activity may concurrently promote healthy HRV through optimizing collaboration between the PNS and SNS and improve quadriceps function.

Therefore, monitoring these two variables is vital for continuing a healthy lifestyle following this traumatic injury to avoid chronic disease.

Similar to the correlation between SDNN and MVIC, higher ratings of the Tegner activity scale had a positive correlation with greater quadriceps strength. In agreement with others, individuals that are not as strong reported hindered levels of physical activity post-ACLR.[19,20] This investigation reinforces the notion that higher quadriceps strength influences higher levels of physical activity. The positive impact on the cardiovascular system is a logical progression of this common finding in the ACLR literature.

We expected that individuals with multiple ACL injuries would present with weaker quadricep strength and less efficient cardiovascular systems compared to those following one ACLR. This hypothesis stands on the basis that more periods of deconditioning would likely further compromise the cardiovascular system. In this analysis, those with 2 ACLRs presented with reduced quadriceps strength and impaired HRV than those with single ACLR. Although these findings were not statistically significant, they still provide the clinician with clinically relevant data to take into consideration during rehabilitation, and while forming short-and long-term goals. The findings of this investigation demonstrate that those with 2 ACLRs were clinically weaker and had less variability when recovering from aerobic exercise. The group mean SDNN was lower than that of the single ACLR group, a trend that describes individuals with 2 ACLRs have less of a PNS influence following exercise. Furthermore, this demonstrates that their SNS is activated longer and their bodies are under stress longer before returning to rest.

There is currently little to no data that considers the relationship between the cardiovascular system and ACLR, and the data that does exist focuses on the short-term months following surgery and rehabilitation.[3,7,8] Almieda et al discovered in the 6 months following ACLR, the cardiovascular systems of those recovering from surgery were significantly impacted when compared to healthy controls.[8] Although these subjects' VO2max values increased following a 6-month rehabilitation protocol, the values were not as high as their presurgical values, or as high as their matched counterparts. Furthermore, Olivier et al discovered in a randomized clinical trial consisting of 24 ACLR individuals and 2 groups: a rehabilitation group with aerobic training for 6 weeks and one without. After testing participants at baseline and after 6 weeks, those in the control group had a lower peak VO2, peak work, peak minute ventilation, second ventilatory threshold, stroke volume, end diastolic volume compared to the rehabilitation group.[3] Both of these studies utilized ventilatory measures in order to examine cardiovascular health, whereas this current study is the first to investigate the long-term effects of ACL injury and reconstruction on HRV. This study provides evidence that HRV is valuable in examining the cardiovascular system in an ACL population. Additionally, HRV provides a non-invasive measure to determine cardiovascular proficiency[21], and it is a valuable tool that could aid further investigation of the cardiovascular system during rest, different types and intensities of exercise, and/or recovery in ACL cohorts. In the long run, this HRV measure could also aid in identifying those who are more at risk for comorbidities in the future depending on the current status of their cardiovascular systems.

This investigation did not include a control group, which could have helped to anchor our ACL data. Additionally, the low sample size of this study (n=14) effects the strength of reliability and generalizability of the findings. A power analysis was not completed for this investigation as this study was highly preliminary, just aiming to identify possible factors affected by ACLR. Lastly, a 12-lead ECG is the gold standard for collecting heart rate data and using the Polar TeamPro could possibly have added artifacts to our data, supplying further room for error as the data analysis software uses estimations to correct these misbeats.

2.6 Conclusion

Our preliminary data suggest that following ACLR, clinicians may need to consider adding cardiovascular fitness as a focus to their rehabilitation protocols. Adjusting the emphasis from a strong strength and neuromuscular focus to including consistent cardiovascular parameters may be critical in returning patients to their full level of activity and cardiovascular health; and continuing this motivation for aerobic activity long after the conclusion of rehabilitation is just as important. This small shift in focus could potentially keep our athletes healthier for longer and could prevent comorbidities in their long-term future.

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2.8 Appendix B

Table 1.

Participants (n)	**14**
Age, years	24 ± 3
Height (cm)	169.67 ± 10.50
Weight (kg)	71.60 ± 17
# of ACLR	
Single ACLR	10
Multiple ACLR	4
Years Post-Op	
Single ACLR	7.2 ± 2.53
Multiple ACLR (1st, 2nd)	8 ± 4.08, 5.5 ± 3

Table 1 – Demographics of participant. (n=14, 9 females and 5 males)

Figure 1.

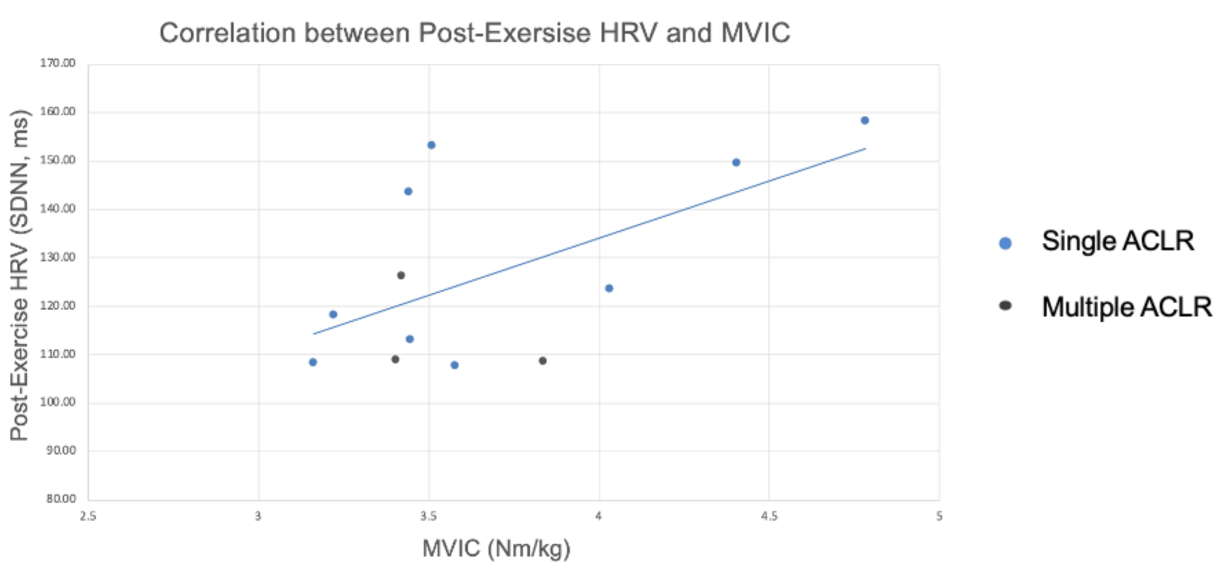

Figure 1 – Pearson correlation between MVIC and HRV, y = 23.584x + 39.789, R=0.599

Figure 2.

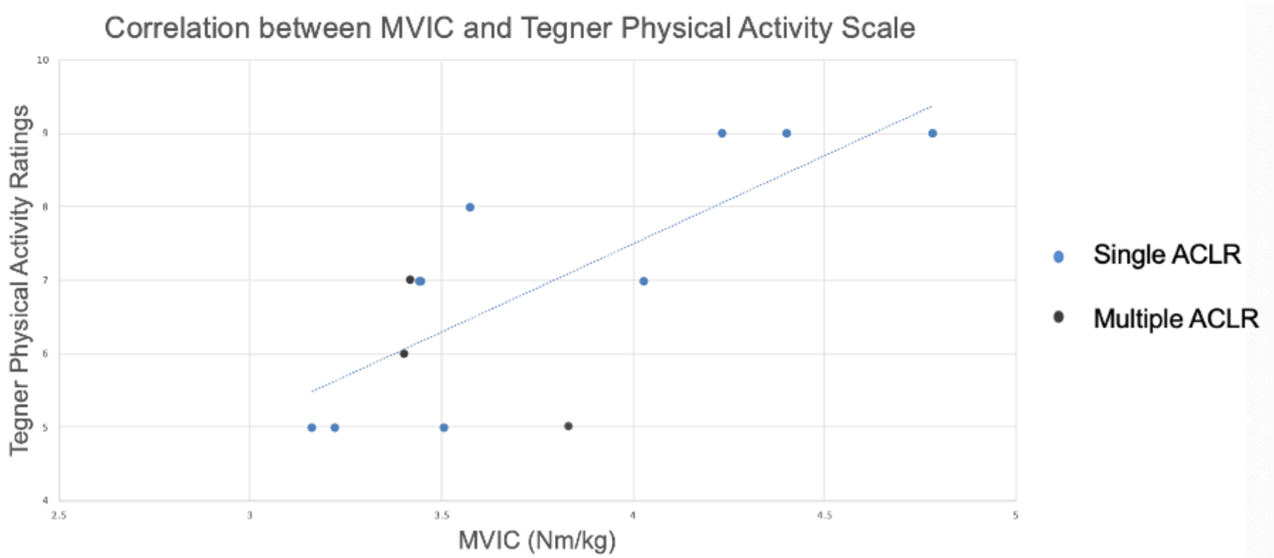

Figure 2 - Pearson correlation between MVIC and Tegner Physical Activity Scale, y = 2.3904x - 2.0634, R=0.751

Table 2.

Group	1 ACLR	Multiple ACLR	Cohen's d effect size	95% Confidence Int.
Mean MVIC	3.906	3.455		
MVIC S.D.	0.499	0.190		
Cohen's d, MVIC			1.00	(-0.41, 2.27)
Mean SDNN	130.73	111.16		
SDNN S.D.	20.411	10.69		
Cohen's d, SDNN			1.07	(-0.24, 2.23)

Table 2 – Mean values and effect sizes for 1 ACLR vs. multiple ACLR