

**PATELLAR TENDINOPATHY:  
OPTIMIZING OUTCOMES OF EXERCISE THERAPY USING A  
COMPREHENSIVE APPROACH TO TENDON HEALTH**

by

Andrew L. Sprague

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

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**DEDICATION**

Dedicated to the Memory of

Forrest Lynn Sprague

Brother, Son, Musician, Environmentalist, and Blue Hen.

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## PREFACE

At the time of publication of this dissertation document, Aim 1 has been published and is reused here with copyright permission of The British Journal of Sports Medicine. I would like to recognize my co-authors and clarify my contribution to this work.

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Angela Hutchinson-Smith, Karin Grävare Silbernagel, and I were jointly responsible for the concept and design of this study, as well as the article screening process. Patrick Knox and I conducted the quality assessment and data extraction. I conducted the data analysis with the statistical expertise of Ryan T Pohlig. All authors assisted with the interpretation of the results and revision of the manuscript.

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## ABSTRACT

Patellar tendinopathy is chronic, painful, overuse injury to the patellar tendon.<sup>1,2</sup> It is rampant among jumping athletes, with 11.8-14.4% of recreational<sup>3</sup> and 32-45% of elite volleyball and basketball players reporting symptoms.<sup>4</sup> These athletes also suffer from impaired function,<sup>5-8</sup> decreased sports performance,<sup>7,9,10</sup> and lost playing time.<sup>7,10-12</sup> Exercise therapy is the treatment with the highest level of evidence.<sup>13,14</sup> This treatment consists of controlled patellar tendon loading, which results in tendon remodeling and ultimately, a reduction of symptoms.<sup>15,16,25,17-24</sup> Although exercise therapy has proven effectiveness, patients only average 52-79% of full recovery following 12 weeks of treatment,<sup>19,20,22,23,26,27</sup> with minimal further improvements at one year.<sup>20,22</sup> Up to one half of these patients will experience reinjury and greater than 50% of those will retire from their chosen sport due to recurrent symptoms.<sup>5</sup>

A singular focus on pain resolution may be to blame for these suboptimal outcomes and high rates of reoccurrence, as resolution of pain does not ensure full recovery of tendon health.<sup>28,29</sup> In addition to pain, patellar tendinopathy is accompanied by alterations in tendon morphology and mechanical properties,<sup>30,31,40,32-39</sup> decreased lower extremity function,<sup>5-8</sup> and impaired quadriceps muscle performance.<sup>41,42</sup> Furthermore, there may be underlying risk factors that contributed to the initial development of the injury.<sup>43-45</sup> These additional impairments and underlying risk factors may not be addressed by patellar tendon loading alone and persist after pain has resolved, acting as a barrier to complete recovery and leaving athletes

vulnerable to reinjury. Therefore, the goal of this dissertation work is to optimize outcomes of exercise therapy for patellar tendinopathy using a comprehensive approach to tendon health. This approach broadens the current pain-focused approach to include other domains of tendon health impacted by the injury.

In the first aim, modifiable risk factors and factors associated with patellar tendinopathy were investigated in a systematic review and meta-analysis.

Identification of modifiable risk factors may lead to new treatment avenues and enhance the effectiveness of treatment and prevention programs. In the second aim, the reliability and stability of continuous shear wave elastography (cSWE) was established for measuring mechanical properties of the patellar tendon. cSWE is a painless, non-invasive form of ultrasound imaging with the ability to measure mechanical properties in-vivo. These properties may be a more responsive measure of tendon health than previously utilized metrics and allow clinicians to better tailor loading to individual patients. In the third aim, relationships between tendon structure (morphology and mechanical properties) and other components of tendon health were investigated. An improved understanding of the role of tendon structure in tendon health may lead to more targeted treatments, which aim to resolve impairments in other domains by addressing the contribution of tendon structure. Finally, the fourth aim examined the feasibility of a randomized clinical trial utilizing pain-guided activity modification during exercise therapy for patellar tendinopathy. Greater activity levels are a risk factor for patellar tendinopathy but clinicians lack guidance on appropriate recommendations for modifying activity during treatment. This work may lead to improved activity modification recommendations that optimize outcomes while maintaining the physical and mental health of athletes.

## Chapter 1

### INTRODUCTION

#### 1.1 Introduction

The patellar tendon extends from the inferior pole of the patella to the tibial tuberosity.<sup>46</sup> During dynamic tasks, the patellar tendon is responsible for transferring forces from the quadriceps muscles to the lower leg, while also acting as a spring to store and release energy.<sup>47,48</sup> The demands placed on the patellar tendon are particularly high in jumping tasks. During a counter-movement jump, the knee extensor mechanism is the primary force generator, performing 41.2% of the work at take-off,<sup>49</sup> and the patellar tendon experiences loads that can exceed six and half times bodyweight upon landing.<sup>50-52</sup> These loads accumulate in sports that require frequent jumping, such as basketball and volleyball, where players perform up to 128 jumps per match.<sup>53-55</sup> Consequently, these athletes are at high risk for developing patellar tendinopathy.

Patellar tendinopathy is the clinical diagnosis of a painful patellar tendon.<sup>1,2</sup> Symptoms are typically isolated to the inferior pole of the patella and are load dependent, with increasing loads resulting in a greater degree of pain.<sup>56</sup> This overuse injury is rampant in jumping sports that place high demands on the patellar tendon, with 11.8-14.4% of recreational<sup>3</sup> and 32-45% of elite volleyball and basketball players reporting symptoms.<sup>4</sup> In addition to pain, these athletes suffer from impaired function,<sup>5-8</sup> decreased sports performance,<sup>7,9,10</sup> and lost playing time.<sup>7,10-12</sup> The consequences of the injury are long-lasting, with symptoms persisting 1.3-2.7 years on

average.<sup>3,4,7</sup> However, many athletes will never fully recover<sup>11,12</sup> and over half of those will retire from sport due to recurrent symptoms.<sup>5</sup>

In addition to pain, patellar tendinopathy is also accompanied by less readily apparent changes to tendon health. Altered tendon morphology, or tendinosis, is typically visible on ultrasound imaging.<sup>30-34</sup> Tendinosis appears as localized tendon thickening, irregular fiber alignment and hypoechoic regions.<sup>31,57</sup> These morphological changes result in altered mechanical properties,<sup>35-40</sup> which influences the tendon's energy storage and force transfer capabilities.<sup>58</sup> These alterations in morphology and mechanical properties contribute to impaired muscle-tendon function.<sup>41,59-62</sup> Furthermore, patellar tendon health may be influenced by pre-existing risk factors, such as additional lower extremity impairments,<sup>63-67</sup> activity levels,<sup>11,68,69</sup> medications,<sup>70,71</sup> genetics,<sup>72,73</sup> systemic diseases<sup>74-80</sup>, or psychological characteristics.<sup>81</sup>

Exercise therapy, consisting of controlled patellar tendon loading, is the initial, primary treatment for patellar tendinopathy.<sup>13,14</sup> The mechanism of action for exercise therapy is mechanotransduction, which is defined as “the process whereby cells convert physiological mechanical stimuli into biomechanical responses”.<sup>15</sup> In the context of exercise therapy for tendinopathy, forces applied to the tendon trigger cellular responses that result in tendon remodeling.<sup>15</sup> In practice, mechanotransduction for the patellar tendon involves knee extension exercises that strengthen the quadriceps muscle and load the patellar tendon. These tendon loading exercises not only result in short-<sup>16,17</sup> and long-term improvements in pain,<sup>16,18-24</sup> but also lead to normalization of tendon structure<sup>20</sup> and mechanical properties,<sup>19,25</sup> and muscle-tendon function.<sup>20,22,24,42</sup>

Although exercise therapy has proven effectiveness, patients only average 52-79% of full recovery following 12 weeks of treatment<sup>19,20,22,23,26,27</sup> with minimal further improvements at one year<sup>20,22</sup> and 27-51% experiencing reinjury.<sup>11,12</sup> Additionally, a subset of patients with patellar tendinopathy do not improve or even worsen during treatment.<sup>22,26,82</sup> There are several potential explanations for these sub-optimal outcomes and the high rates of reoccurrence. First, patellar tendon loading alone may not address underlying risk factors that contributed to the initial development of the injury.<sup>43-45</sup> These risk factors can persist after treatment, acting as a barrier to complete recovery and predisposing athletes to re-injury. Second, the primary goal of most treatment protocols is pain resolution.<sup>18,22,27,82</sup> However, the absence of pain does not ensure full recovery of morphology, mechanical properties, or muscle-tendon function.<sup>28,83</sup> Thus, treatment focused solely on pain resolution leaves patients vulnerable to re-injury. Third, activity modification during treatment may be insufficient,<sup>82</sup> limiting the tendon's ability to recover between bouts of loadings, or overly conservative,<sup>21,22,24</sup> diminishing the tendon's tolerance to sport specific loading. As a result, the benefits of treatment may be blunted or athletes may not be prepared to return to sports activity.

Therefore, the goal of this dissertation work is to optimize outcomes of exercise therapy for patellar tendinopathy using a comprehensive approach to tendon health. To achieve this goal, the following aims will be addressed:

**Aim 1:** Identify potential modifiable risk factors and modifiable factors associated with patellar tendinopathy through a systematic review and meta-analysis of current literature.

**Aim 2:** Establish stability and reliability of cSWE to evaluate the mechanical properties of the patellar tendon.

**Aim 3:** Explore the relationships between patellar tendon structure (morphology and mechanical properties) and injury severity, lower extremity performance and quadriceps muscle function in patellar tendinopathy.

**Aim 4:** Determine the feasibility of a randomized clinical trial utilizing pain-guided activity modification while undergoing treatment for patellar tendinopathy.

Ultimately, knowledge gained from this work will result in enhanced treatment programs for patellar tendinopathy that may enhance recovery and reduce re-injury, and allow clinicians to provide more tailored load prescription and activity modification. Furthermore, utilizing a comprehensive approach to tendon health will increase awareness of the presence and consequences of impairments in tendon health that extend beyond pain and symptoms.

## **1.2 Risk Factors for Patellar Tendinopathy**

A potential limitation of current patellar tendon treatment protocols is that they are comprised solely of tendon loading exercises. Although these exercises are the cornerstone of patellar tendinopathy treatment, these patients often have other impairments or behaviors that contributed to the initial development of the injury and may not be addressed by tendon loading.<sup>44,45</sup> These risk factors may be a barrier to complete recovery and may persist after treatment, increasing the likelihood of reinjury. Furthermore, identifying and addressing risk factors prior to injury may prevent the development of patellar tendinopathy, so athletes never enter a cycle of recurrent pain and functional limitation.

A previous systematic review by van der Worp *et al* identified over 40 potential or proposed risk factors for patellar tendinopathy, but only nine had sufficient evidence to be considered of interest in rehabilitation and prevention programs (weight, body mass index, waist-to-hip ratio, leg-length difference, arch height of the foot, quadriceps flexibility, hamstring flexibility, quadriceps strength and vertical jump performance).<sup>44</sup> Furthermore, many proposed risk factors had not been prospectively investigated, had limited support from low-quality studies or had conflicting evidence.<sup>44</sup> Since the publication of van der Worp *et al's* systematic review in 2011, there has been an exponential increase in research directly or indirectly investigating risk factors for patellar tendinopathy. Since 1973, when patellar tendinopathy was first described,<sup>56</sup> to van der Worp *et al's* systematic review, there were 166 published articles on PubMed with patellar tendinopathy, or its synonyms, in the title. In the following decade, 244 further articles have been added. This expansion of the literature regarding patellar tendinopathy may provide additional evidence for previously unsupported risk factors or identify new risk factors for the injury.

However, all proposed risk factors are not modifiable. Therefore, they may assist in identifying athletes at increased risk of injury but do not provide an avenue for clinicians to intervene and reduce that risk. For example, Morton *et al* recently investigated the relationship between the presence of patellar tendinopathy and variety of potential risk factors.<sup>65</sup> Female sex, training greater than 20 hours per week, previous knee injuries and more flexible hamstrings were significantly associated with the presence of patellar tendinopathy. Of these potential risk factors, only training load and hamstring flexibility may be altered by clinicians, so sex and injury history may be of less interest in clinical decision-making during treatment.

Therefore, the purpose of Aim 1 is to identify modifiable risk factors for patellar tendinopathy through a systematic review and meta-analysis of current literature. Building upon the work of van der Worp *et al*, this aim will identify the risk-factors of interest to address in rehabilitation and prevention programs. Furthermore, performing a meta-analysis may provide further clarity for risk factors with conflicting evidence.

**Aim 1:** Identify potential modifiable risk factors and modifiable factors associated with patellar tendinopathy through a systematic review and meta-analysis of current literature.

**Aim 1.1:** Identify potential modifiable risk factors for patellar tendinopathy.

**Aim 1.2:** Identify modifiable factors associated with patellar tendinopathy.

### **1.3 Evaluating Mechanical Properties in Patellar Tendinopathy**

The goal of exercises therapy is to promote tendon remodeling, improve the tendon's tolerance to load, and reduce symptoms. To be effective, the prescribed loads must be adequate to promote structural remodeling<sup>84</sup> without excessive overload, which can result in further tendon degeneration and worsening of symptoms.<sup>85-87</sup> Load can be increased by changing the resistance, repetitions, duration, or speed of the exercises.<sup>86</sup> Current treatment protocols rely on a variety of methods for initial load prescription and progression.<sup>18-22,24,27,88</sup> However, it is unclear if these methods are optimal since our ability to assess a tendon's response to a bout or bouts of loading is limited. Improved methods to determine the appropriateness of load prescription are needed, which allow clinicians to tailor loads for individual patients.

Traditionally, symptoms have been the primary guide to load prescription,<sup>21,27</sup> yet, symptoms do not account for changes in tendon structure. To evaluate structural remodeling, changes in both morphology and mechanical properties have been proposed. Morphology, such as tendon thickness and cross-sectional area, is typically assessed via B-mode ultrasound. However, morphological changes occur slowly so B-mode ultrasound imaging has limited utility in determining the short-term response to tendon loading.<sup>20,89,90</sup> Tendon mechanical properties may be a more responsive measure of tendon health and may provide rapid feedback on the appropriateness of prescribed loads.<sup>91,92</sup> Until recently, methods for assessing mechanical properties have been invasive<sup>93-96</sup> or rely on muscle activation,<sup>38</sup> which is unreliable in the presence of pain.<sup>97</sup> Our research group has developed a painless, non-invasive technique called Continuous Shear Wave Elastography (cSWE) that does not require muscle contraction and has the ability to quantify mechanical properties in-vivo.<sup>91</sup>

cSWE is a form of ultrasound imaging which utilizes an external vibration to transmit shear waves through the tendon.<sup>91</sup> These waves are recorded by an ultrasound probe and the recordings are used to determine the mechanical properties of the tendon (shear modulus, and viscosity). Recently, commercial elastography systems have been developed but these systems lack the measurement range required for use in relatively stiff tendon,<sup>98,99</sup> are unable to provide quantitative values,<sup>100</sup> or use a burst of unspecified frequencies to generate a shear wave.<sup>91</sup> In the later limitation, lack of a set frequency for shear wave generation means that values obtained can only be considered a rough estimation of mechanical properties. cSWE is not hindered by these limitations, has been found to be valid and reliable for the Achilles tendon, and

provides additional metrics of mechanical properties. However, reliability has not been established for the patellar tendon.

Therefore, Aim 2 seeks to establish the stability and reliability of cSWE at the patellar tendon. The ability to reliably measure patellar tendon mechanical properties with cSWE may provide more timely feedback on a tendon's response to loading and a more complete picture of tendon health, allowing a more tailored approach to load prescription.

**Aim 2:** Establish stability and reliability of cSWE to evaluate the mechanical properties of the patellar tendon.

**Hypothesis 2.1:** Intra- and inter-rater reliability of the procedure for shear modulus and viscosity will be moderate to good ( $ICC \geq 0.6-0.75$ ).

**Hypothesis 2.2:** Between days stability for shear modulus and viscosity will be good ( $ICC \geq 0.5$ ).

**Hypothesis 2.3:** Smallest detectable change (SDC) values at the group level for mechanical properties will be less than or equal to values reported for the Achilles tendon (static shear modulus  $\leq 6.0$  kPa and viscosity  $\leq 3.8$  Pa\*s).

#### **1.4 Relationships between Tendon Structure and other Components of Tendon Health**

The constituents of tendon health comprise an interrelated system.<sup>29</sup> This has been clearly demonstrated in individuals with Achilles tendinosis.<sup>29</sup> Alterations in Achilles tendon structure, both morphology and mechanical properties, contribute to changes in motor system control, resulting in reduced triceps surae activity and functional performance in the absence of pain.<sup>29</sup> Therefore, Achilles tendon structure

drives changes in other levels of this system. Yet, these relationships are less clear for the patellar tendon. An improved understanding of the role of tendon structure in patellar tendon health may help explain the presence of clinical impairments. Furthermore, it will result in more targeted treatments, which aim to resolve these impairments by addressing the contribution of altered tendon structure.

Several studies have attempted to explore the relationships between patellar tendon structure and other components of tendon health, to various degrees. In healthy individuals mechanical properties relate to jump performance.<sup>101</sup> Abnormal tendon morphology is associated with a fourfold increased risk of developing patellar tendinopathy, however, morphological changes correlate poorly with clinical symptoms.<sup>102–106</sup> This is expected, given the fact that morphological changes occur slowly and persist after symptom resolution.<sup>20,89,90</sup> In patellar tendinopathy, mechanical properties and changes in these properties following treatment relate to pain and patient-reported symptom severity.<sup>25,35,40,107</sup> Still, the presence of these relationships,<sup>108,109</sup> and their strength<sup>25,107</sup> or direction varies between studies.<sup>25,35</sup> This is likely due to methodological differences between studies, such as the technique used for measuring mechanical properties or the parameters reported. Tendon morphology and mechanical properties relate to measures of quadriceps muscle function in healthy individuals<sup>110</sup> and central nervous system input to the quadriceps is altered in patellar tendinopathy.<sup>41</sup> Despite these findings and the evidence that tendon structure affects agonist muscle activity in Achilles tendinopathy, the relationship between structure and quadriceps muscle activity in patellar tendinopathy remains unexplored. Cumulatively, these previous studies suggest that patellar tendon structure may

influence other areas of tendon health but the role of tendon structure requires further investigation.

Therefore, Aim 3 will explore the relationships between patellar tendon structure and injury severity, lower extremity function and quadriceps muscle performance in individuals with patellar tendinopathy. Identifying how patellar tendon structure relate to these other metrics will improve our understanding of tendon health and lead to more effective treatments.

**Aim 3:** Explore the relationships between patellar tendon structure (tendon morphology and mechanical properties) and symptom severity (Victorian Institute of Sport Assessment – Patellar questionnaire), lower extremity function (counter-movement jump and drop counter movement jump height) and quadriceps muscle performance (knee extension peak force and quadriceps central activation ratio) in individuals with patellar tendinopathy.

**Hypothesis 3.1:** Tendon morphology (thickness and cross-sectional area) will not relate to symptom severity, lower extremity function but will relate to quadriceps muscle performance.

**Hypothesis 3.1a:** There will be no significant relationship between tendon morphology and symptom severity.

**Hypothesis 3.1b:** There will be no significant relationship between tendon morphology and lower extremity function.

**Hypothesis 3.1c:** Tendon thickness and cross-sectional area will negatively relate to peak knee extension force but not quadriceps central activation ratio.

**Hypothesis 3.2:** Tendon mechanical properties will relate to symptom severity, lower extremity function and quadriceps muscle performance.

**Hypothesis 3.2a:** Tendon mechanical properties (static shear modulus and viscosity) will positively relate to symptom severity.

**Hypothesis 3.2b:** Tendon mechanical properties will negatively relate to lower extremity function.

**Hypothesis 3.2c:** Tendon mechanical properties will negatively relate to quadriceps muscle performance.

### **1.5 Role of Activity Modification in Patellar Tendinopathy**

Activity modification is considered a requirement of successful exercise therapy,<sup>2</sup> since high levels of activity have been implicated as a causative factor in patellar tendinopathy.<sup>11,68,111</sup> This is unsurprising, as tendinopathy is typically an overuse injury and most common in athletes.<sup>56</sup> Activity modification involves changing the patient's type, duration and/or intensity of activity outside of treatment to ensure the tendon has adequate time for recovery between bouts of loading.<sup>112</sup> Following heavy loading, the tendon may require up to 72 hours to fully recover.<sup>113</sup> Although modification of activity is considered necessary, activity modification recommendations have not been directly investigated or compared.

The implementation of activity modification in studies of exercise therapy for patellar tendinopathy varies widely. Protocols have achieved positive results using either complete cessation of sports participation<sup>21,22,24</sup> or a more graded approach with pain-guided activity modification.<sup>19,20</sup> Additionally, three previous studies have investigated the effectiveness of exercise therapy without activity modification, with

mixed results.<sup>17,18,82</sup> One study found a protocol of eccentric decline squats to be ineffective when patients continued participating in sport at their pre-injury level.<sup>82</sup> The other studies found 4-week protocols of isometric or isotonic tendon loading to improve pain and function without altering activity, which calls into question whether activity modification is truly needed.<sup>17,18</sup> However, since the impact of activity modifications on treatment outcomes has not been examined, it is unclear whether the extent of activity modification was beneficial or detrimental to treatment outcomes.

It is likely that the optimal amount of activity modification lies somewhere between activity cessation and full participation, as either end of the spectrum may have negative consequences. Absence from sport due to injury has been associated with increased anxiety, depression and reduced self-esteem.<sup>114</sup> Furthermore, withdrawal from sports may reduce the tendon's tolerance to sport-specific loading and the patient's physical fitness, making them susceptible to re-injury. Conversely, full participation may reduce or nullify the benefits of exercise therapy.<sup>82</sup> Therefore, it is of interest to identify a middle ground, which minimizes the negative psychological consequences while promoting recovery. In a prior randomized clinical trial (RCT), our research group established that continued activity during treatment, using pain-guided activity modification, had no detrimental effects on outcomes of treatment in Achilles tendinopathy when compared with pain-free activity modification.<sup>115</sup>

Although, pain-guided activity modification has been used in patellar tendinopathy, the impact of this approach on treatment outcomes has not been investigated or compared with other recommendations. Prior to performing a large RCT to compare the effectiveness of pain-guided activity modification with other recommendations, it is crucial to establish the feasibility of the planned

interventions.<sup>116</sup> Since patellar tendinopathy is common in team sports, using individualized activity recommendations may pose unforeseen challenges.

Therefore, the purpose of Aim 4 is to determine the feasibility of a randomized clinical trial utilizing pain-guided activity modification while undergoing treatment for patellar tendinopathy. Findings of this work will set the stage for a larger RCT, which may improve activity modification recommendations, leading to accelerated recovery and improved patient outcomes.

**Aim 4:** Determine if it is feasible to conduct a randomized clinical trial utilizing pain-guided activity modification during treatment for patellar tendinopathy.

**Aim 4.1:** Examine access to potential participants, percentage of potential participants meeting inclusion criteria, percentage of eligible participants that are willing to be randomized, monthly recruitment and retention.

**Aim 4.2:** Examine the compliance of participants with treatment, activity modification and training diaries.

**Hypothesis 4.1:** Symptom severity, degree of altered tendon mechanical properties, lower extremity function, and quadriceps muscle performance, but not tendon morphology, will improve significantly in both groups.

## **1.6 Summary**

Patellar tendinopathy is a chronic, painful injury to the patellar tendon with consequences that extend beyond the primary complaints of pain and stiffness.<sup>5-12</sup> Typically sports related,<sup>3,4</sup> the injury beleaguers athletes for years,<sup>3,4,7</sup> often leading to

retirement from sports participation.<sup>5</sup> Exercise therapy is currently the treatment with the highest level of evidence for patellar tendinopathy<sup>13,14</sup> but, even with treatment, many patients do not achieve full recovery<sup>19,20,22,23,26,27</sup> and up to half will experience re-injury.<sup>11,12</sup> These patients have been disserved by a treatment paradigm that focuses solely on pain resolution, while ignoring impairments in other constituents of tendon health.<sup>30,31,40,41,59-62,32-39</sup> Resolution of symptoms does not ensure full recovery of tendon health.<sup>28,29</sup> Therefore, this approach may be a barrier to full recovery and predispose athletes to re-injury. This dissertation work aims to optimize outcomes of exercise therapy for patellar tendinopathy using a comprehensive approach to tendon health. The knowledge gained may improve our understanding of patellar tendon health and empower clinicians with the ability to better tailor load prescription and activity modification to the individual, leading to accelerated recovery and lower rates of re-injury.

## Chapter 2

### MODIFIABLE RISK FACTORS FOR PATELLAR TENDINOPATHY IN ATHLETES: A SYSTEMATIC REVIEW AND META-ANALYSIS

#### 2.1 Introduction

Patellar tendinopathy is a clinical diagnosis, characterized by focal pain at the inferior pole of the patella and load-dependent symptoms, with increased loads resulting in a greater degree of pain.<sup>2</sup> It most commonly affects athletes participating in jumping sports, where the extensor mechanism experiences high, repetitive loads.<sup>4</sup> The prevalence of patellar tendinopathy is high, with 11.8-14.4% of recreational volleyball and basketball players reporting symptoms.<sup>3</sup> In elite players the prevalence is even higher, with 32% of elite men's basketball players and 45% of elite men's volleyball players experiencing symptoms.<sup>4</sup> These players have decreased sports performance<sup>4</sup> and prolonged absences from training and matches.<sup>12</sup> Although many athletes with patellar tendinopathy will seek treatment or modify activity, 49% will experience recurrent symptoms<sup>12</sup> and more than 50% may retire from sports participation due to persistent pain.<sup>5</sup> Therefore, it is of interest to identify ways to prevent patellar tendinopathy so athletes never enter a cycle of recurrent pain and functional limitation.

Identification of risk factors for patellar tendinopathy is essential to development of targeted prevention programs. A previous systematic review by van der Worp et al. identified over 40 potential risk factors for patellar tendinopathy.<sup>44</sup> However, the authors found that many proposed risk factors have not been

prospectively investigated, have limited support from low-quality studies or have conflicting evidence. Additionally, not all risk factors were modifiable. Thus, they may assist in identifying athletes at higher risk of injury but do not provide an opportunity for clinicians to intervene to reduce that risk. Building upon the work by van der Worp et al., the purpose of this study was two-fold:

1. To systematically identify potential modifiable risk factors for patellar tendinopathy in athletes using prospective, longitudinal studies.
2. To systematically identify associated modifiable factors in athletes, which lack prospective support as potential modifiable risk factors, using cross-sectional studies.

## **2.2 Methods**

The protocol for this review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (ID #: 42016052904) and conducted according to Preferred Reporting Items for Systemic Reviews and Meta-Analysis (PRISMA) guidelines.<sup>117</sup>

## **2.3 Search Strategy**

Using the assistance of a research librarian, a search strategy was developed based on two categories of interest: (1) terms related to the patellar tendon or patellar tendinopathy and (2) terms related to modifiable risk factors (Figure 2.1). A human participants restriction was applied. Studies were not limited to a specific time period or language. Preliminary searches were conducted to ensure that the search strategy was comprehensive. Following preliminary searches, articles including the terms “ACL”, “anterior cruciate ligament”, “graft”, “arthroplasty”, “prosthetic” and “fracture” in their title or abstract were excluded to limit the number of irrelevant

articles. An online search was performed of PubMed, Web of Science, Scopus and CINAHL. The initial search was conducted on 18 November 2016 and repeated on 14 November 2017. Following the full-text review phase, references of included studies and retained systematic reviews were hand-searched for additional relevant articles not captured by the initial search.

<p><b>a)</b></p> <p>(((((patellar tendon OR patella tendon OR patella tendinopathy OR patellar tendinopathy OR patella tendinosis OR patellar tendinosis OR patella tendinitis OR patellar tendinitis OR patella apicitis OR patellar apicitis OR patella tenosynovitis OR patellar tenosynovitis OR jumper's knee)))) AND ((risk factor OR relative risk OR odds OR probability OR prevalence OR odds ratio))) NOT ("ACL"[Title/Abstract] OR "anterior cruciate ligament"[Title/Abstract] OR "graft"[Title/Abstract] OR "arthroplasty"[Title] OR "prosthetic"[Title] OR "fracture"[Title]) AND (Humans[Mesh])</p>
<p><b>b)</b></p> <p>(patellar tendon OR patella tendon OR patella tendinopathy OR patellar tendinopathy OR patella tendinosis OR patellar tendinosis OR patella tendinitis OR patellar tendinitis OR patella apicitis OR patellar apicitis OR patella tenosynovitis OR patellar tenosynovitis OR jumper's knee) AND (risk factor OR relative risk OR odds OR probability OR prevalence OR odds ratio) NOT ("ACL" OR "anterior cruciate ligament" OR graft OR arthroplasty OR prosthetic OR fracture*) <i>Human limit Applied</i></p>
<p><b>c)</b></p> <p>(patellar tendon OR patella tendon OR patella tendinopathy OR patellar tendinopathy OR patella tendinosis OR patellar tendinosis OR patella tendinitis OR patellar tendinitis OR patella apicitis OR patellar apicitis OR patella tenosynovitis OR patellar tenosynovitis OR jumper's knee) AND (risk factor OR relative risk OR odds OR probability OR prevalence OR odds ratio) NOT ("ACL" OR "anterior cruciate ligament" OR graft OR arthroplasty OR prosthetic OR fracture*) NOT (Dog* or Rats OR canine*)</p>
<p><b>d)</b></p> <p>(ALL((patellar tendon OR patella tendon OR patella tendinopathy OR patellar tendinopathy OR patella tendinosis OR patellar tendinosis OR patella tendinitis OR patellar tendinitis OR patella apicitis OR patellar apicitis OR patella tenosynovitis OR patellar tenosynovitis OR jumper's knee OR (patella* AND tendinopath*))) AND (TITLE-ABS-KEY((risk factor*))OR TITLE-ABS-KEY(relative risk* OR odds OR probability OR prevalence OR odds ratio*))) AND NOT TITLE-ABS("ACL" OR "anterior cruciate ligament" OR graft OR arthroplasty OR prosthetic OR fracture*) AND NOT TITLE-ABS(Dog* OR rats OR canine*)</p>

Figure 2.1: Search strategies utilized for (a) PubMed, (b) CINAHL, (c) Web of Science, and (d) Scopus.

### 2.3.1 Inclusion and exclusion criteria

All quantitative original research comparing athletes with patellar tendinopathy to a control group without the injury was considered. Patellar tendinopathy is defined as symptoms isolated to the inferior pole of the patella.<sup>2</sup> However, historically, patellar tendinopathy was more broadly defined as “Jumper’s Knee” and included symptoms

anywhere along the patellar tendon or quadriceps tendon.<sup>118</sup> Therefore, studies that utilized a broader definition of patellar tendinopathy were included, as symptoms at sites other than the inferior pole of the patella are less common.<sup>118</sup> Studies in which diagnosis was based on imaging alone were excluded since patellar tendon structural changes are common in individuals without clinical signs and symptoms of patellar tendinopathy.<sup>106</sup> Animal, cadaveric or interventional studies were excluded. Abstracts, conference proceeding, editorials, opinion-based papers, reviews (narrative or systematic), letters, case series and case studies were also excluded. However, systematic reviews were retained until the full-text phase so their references could be included in the hand-search. Additionally, studies lacking modifiable potential risk factors or associated factors, or a clear comparison between patellar tendinopathy and a group without the injury were excluded.

### **2.3.2 Study selection**

Prior to record screening, duplicates were removed by the research librarian. Two reviewers (ALS and AHS) completed title, abstract and full-text review independently for all records. Records were screened for inclusion/exclusion criteria. After each phase of the screening process, disagreements regarding record inclusion were discussed and a third reviewer (KGS) was consulted if consensus could not be reached. Included articles were grouped based on study design; prospective, longitudinal, cohort studies (prospective) and cross-sectional or case-control studies (cross-sectional). Prospective studies can identify potential modifiable risk factors, since presence or exposure to the risk factor are determined prior to development of patellar tendinopathy. At best, items identified in cross-sectional studies can only be

considered associated modifiable factors, since a temporal relationship cannot be established.

### **2.3.3 Quality assessment**

Studies were independently assessed for risk-of-bias and methodological quality by two reviewers (ALS and PK) using a modified version of the Newcastle-Ottawa Scale (NOS).<sup>119</sup> The NOS is an eight-item checklist, grouped into three domains (selection, comparability, and outcome or exposure) designed for assessing risk-of-bias in non-randomized studies. There are two versions of the instrument, one for case-control (cross-sectional) studies and one for cohort (prospective) studies. For each item assessed, a list of responses is provided and the reviewer must select the response most appropriate for the study. Responses that indicate low risk-of-bias are awarded a star and studies can receive a maximum score of nine stars. For certain items, multiple responses may be appropriate. For example, studies that reported multiple factors of interest may have used independent blind assessment for some factors and self-report for others. In these instances, separate scores are reported. The NOS has been previously used for quality assessment in systematic reviews<sup>81,120</sup> and was deemed appropriate for use in a review of quality assessment instruments.<sup>121</sup> If reviewers disagreed on a quality assessment rating, the inconsistency was discussed and a third reviewer (KGS) was consulted, if necessary, to resolve disputes. Studies were not excluded based on their quality assessment score. However, the quality assessment score was considered for determining the strength of the results.

#### **2.3.4 Data extraction**

Data extraction was completed by a single reviewer (ALS) using pre-defined categories and independently verified by a second reviewer (PK). These categories included: study design, potential risk factors investigated, inclusion and exclusion criteria, group allocation, sample size, population age, sports included, competition level, sex distribution, proportion of cases and controls, diagnostic criteria for patellar tendinopathy and study conclusions. For each factor of interest, the method of measurement, reported values, statistical test used and significance level were also recorded. Factors were excluded from analysis if they were used for matching case and control groups, as the distribution of these factors were controlled by the research team and cannot be attributed to the injury. Additionally, factors previously reported in a study using the same or part of the same sample were excluded to prevent data duplication. Ultrasound imaging measures and biomechanical variables were not extracted since these measures were recently explored in other systematic reviews.<sup>102,122</sup> Potential risk factors or factors associated with patellar tendinopathy were categorized into six groups:

- Anthropometrics
- Joint Range-of-Motion and Muscle Length
- Sports and Physical Activity
- Functional Test Performance
- Muscle Performance
- Occupational Demands

### 2.3.5 Data synthesis and analysis

Cohen's Kappa values were calculated for inter-rater agreement for each stage of the screening process and for quality assessment ratings.<sup>123</sup> Scores were interpreted using pre-defined cut-off scores.<sup>124</sup>

For potential risk factors or associated factors reported by five or more studies within a study-design grouping, meta-analytic statistics are reported. Cohen's *d* with 95% confidence intervals were calculated for each factor using Comprehensive Meta-Analysis software, version 3.3.070 (Engelwood, NJ, USA) with alpha set at 0.05.<sup>125</sup> A positive effect indicates that the measured value was larger in the patellar tendinopathy group and a negative effect indicates the value was smaller in the patellar tendinopathy group. As a follow-up, odds ratios ( $OR = ((n) \text{ exposed cases} / (n) \text{ unexposed cases}) / ((n) \text{ exposed controls} / (n) \text{ unexposed controls})$ ) with 95% confidence intervals are reported for significant effects.<sup>126</sup> For calculation of effect sizes the fixed effects model was used when heterogeneity between studies was low or moderate and random effects model used when it was high. This study followed McAuliffe et al's<sup>102</sup> criteria for assessing heterogeneity using Higgin's  $I^2$  value,<sup>127</sup> an  $I^2 \leq 30\%$  was considered low and  $I^2 > 30\%$  was moderate; heterogeneity was high when  $I^2 > 50\%$ .

Funnel plots<sup>128</sup> were created and analyzed for publication bias using Duval and Tweedie's Trim and Fill method for all factors reported in the quantitative synthesis.<sup>129</sup> If a factor of interest was reported separately for unilateral and bilateral tendinopathy, sex, or limb then the weighted pooled mean and variance was used in the analysis. In some studies, several measures of the same outcome were reported. In these cases, the weighted pooled mean and variance were also used to obtain a combined measure of effect. If a factor was discussed but insufficient data was

reported to calculate a measure of effect, then the authors were contacted to request additional information.

Studies or factors not included in the meta-analysis were included in the qualitative summary. The strength of evidence for factors of interest was assessed using criteria established by Mallows et al. to synthesize non-randomized studies.<sup>81</sup> Each study was assigned a quality assessment score by dividing the stars awarded on the NOS by the number of available stars. Based on these scores, studies were classified as low (0.00-0.44, 1-4 stars), moderate (0.45-0.70, 5 or 6 stars), or high quality (0.71-1.00, 7-9 stars).<sup>81</sup> A rating system, adapted by Mallows et al.<sup>81</sup> from the Cochrane Collaboration Back Review Group,<sup>130</sup> was used to rate the level of evidence for each factor of interest, accounting for the quality and quantity of evidence (Table 2.1). A study was considered to have positive findings if significance testing was performed and the p-value was less than 0.05.

Table 2.1: Levels of Evidence

<b>Strong evidence</b>	Consistent findings in high-quality studies (n≥2)
<b>Moderate evidence</b>	Consistent findings among lower-quality studies (n>2) and/or one high-quality study
<b>Limited evidence</b>	(n≤2) relevant lower-quality studies
<b>Conflicting evidence</b>	Inconsistent findings among multiple studies
<b>No evidence</b>	No studies with significant findings

## 2.4 Results

### 2.4.1 Identification of studies

The initial search resulted in 862 studies (Figure 2.2). After removal of duplicates, 768 records were screened for inclusion and exclusion criteria. Following

title and abstract review, 133 studies were appropriate for full-text review. 107 studies were excluded during full-text review, yielding 26 articles for inclusion. Inter-rater agreement ranged from moderate to almost perfect (Table 2.2). Five additional articles were included after hand-searching references of included articles and retained systematic reviews, resulting in 31 included articles for qualitative review (Figure 2.1). Of these articles, 28 contained factors that were included in the quantitative synthesis (Figure 2.2). All included articles were in English. Authors provided additional information for five of eight articles for which additional information was requested.

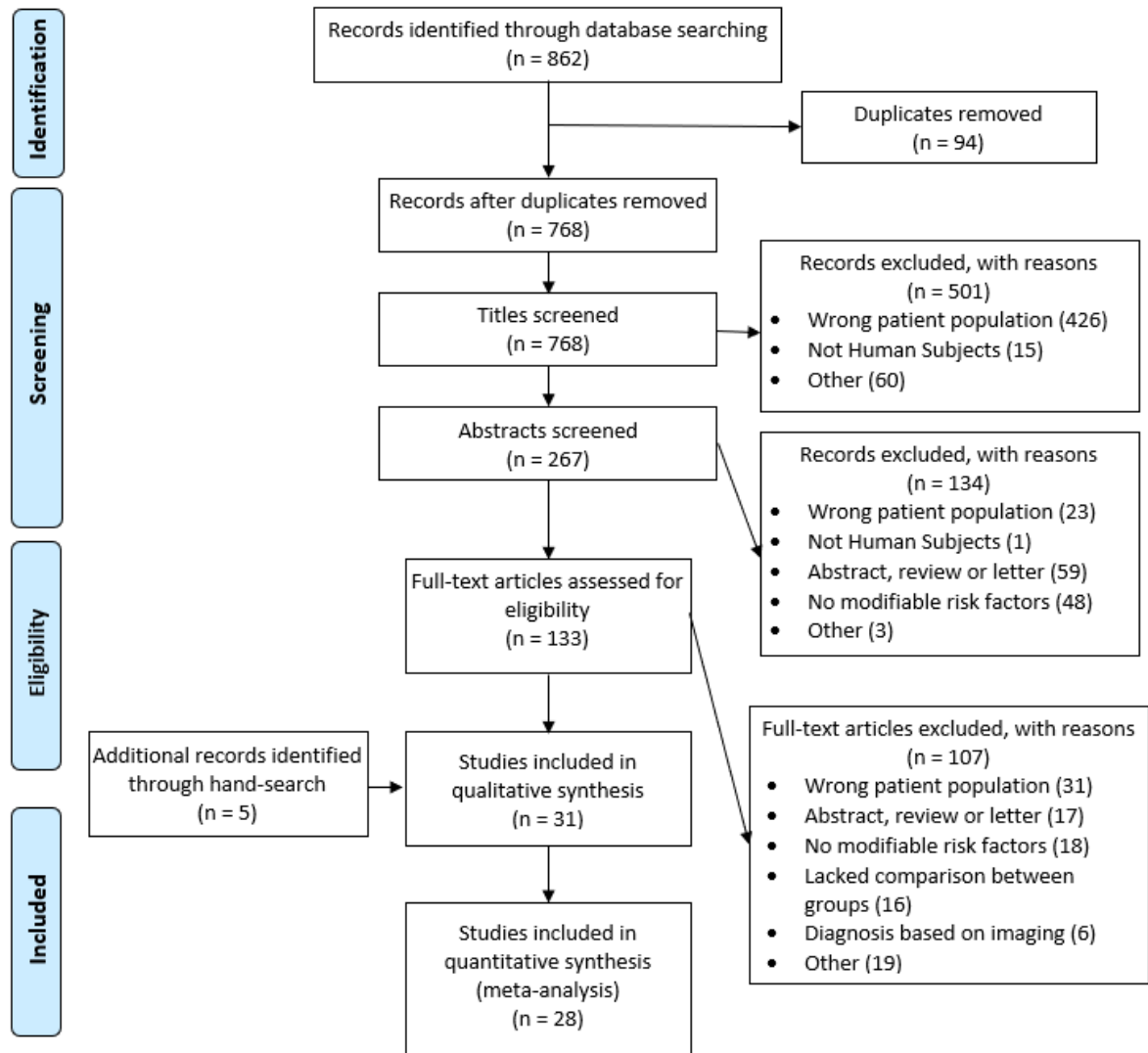


Figure 2.2: PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Table 2.2: Cohen’s Kappa values for inter-rater agreement of record screening and quality assessment.

Screening or Assessment Stage	Cohen’s Kappa ( $\kappa$ )
Title Screening	0.904
Abstract Screening	0.491
Full-Text Screening	0.701
Quality Assessment	0.744

#### **2.4.2 Study Characteristics**

Of the 31 studies considered, six were prospective. All six included young athletes, with mean ages under 30. The majority, 83% (5/6), played either volleyball or basketball, and consisted of elite athletes competing at the professional, national or international level (67%, 4/6) (Table 2.3). Twenty-five studies were cross-sectional, and similarly 88% (22/25) had mean ages less than 30 years old. The majority of athletes were volleyball and basketball players (80%, 20/25); however only 32% (8/25) included elite athletes (Table 2.3). The majority of prospective (86%, 6/7) and cross-sectional (56%, 14/25) studies included both sexes although, 40% (10/25) of cross-sectional studies consisted of only male athletes (Table 2.3).

Table 2.3: Characteristics of included studies.

Study	Potential Risk Factors Investigated	Diagnostic Criteria	Sample Size (Injured/Uninjured)	Sport and Competition Level	Mean Age (SD) (Years)*	Sex (Male/Female)
<b>Prospective Studies</b>						
<b>Backman et al. (2011)</b> <sup>♦131</sup>	BMI, BW, Ankle dorsiflexion ROM, Activity volume, Sport-specific training volume	<ol style="list-style-type: none"> <li>1) History of activity related anterior knee pain.</li> <li>2) Distinct palpation tenderness corresponding to painful area.</li> <li>3) Knee pain provoked by single-legged decline squat</li> </ol>	75 (12/63)	Basketball players competing at the national elite level.	17.8 (1.6)	38/37
<b>de Vries et al. (2015)</b> <sup>♦132</sup>	BMI, BW, Activity volume, Other sports training volume, Playing surface, Occupational classification, Occupational demands	<ol style="list-style-type: none"> <li>1) Indicated pain at the inferior pole of the patella on a self-administered pain map.</li> <li>2) And/or physician or physical therapist had diagnosed the knee problem as patellar tendinopathy.</li> </ol>	385 (51/334)	Basketball and volleyball players competing at the elite (regional or national) or non-elite level.	28.3 (4.5)	142/243
<b>Hagglund et al. (2011)</b> <sup>♦11</sup>	BW, Activity and playing volume, Training/match exposure ratio, Playing surface	Diagnosis based on clinical examination by the team medical staff but no specific diagnostic criteria provided.	2229 (137/2,092)	Soccer players competing at the professional level.	UCL: 25.7 (4.5); SWE: 24.8 (4.7); ART: 25.0 (4.8)	All male

Table 2.3 continued.

<b>Visnes and Bahr (2013)*<sup>68</sup></b>	BW, Waist circumference, Skinfold measurements, Volleyball sets per week, Beach volleyball training volume, Strength training volume, Jump training volume, Other training volume	<ol style="list-style-type: none"> <li>1) History of pain in the quadriceps or patellar tendons at their patellar insertion in connection with training or competition.</li> <li>2) Tenderness to palpation corresponding to the painful area.</li> </ol>	141 (28/113)	Volleyball players competing at the elite level.	16.8 (0.8)	69/72
<b>Visnes et al. (2013)<sup>111</sup></b>	CMJ height, Standing jump height	<ol style="list-style-type: none"> <li>1) History of pain in the quadriceps or patellar tendons at their patellar insertion in connection with training or competition.</li> <li>2) Tenderness to palpation corresponding to the painful area.</li> </ol>	150 (28/122)	Volleyball players competing at the elite level.	16.7 (0.8)	68/82
<b>Witvrouw et al. (2001)*<sup>63</sup></b>	BW, Posterior thigh flexibility, Quadriceps flexibility, Peak normalized isokinetic knee extension torque (60, 180 and 240 deg/sec), Peak normalized isokinetic knee flexion torque (60, 180, and 240 deg/sec)	<ol style="list-style-type: none"> <li>1) Characteristic history of pain in the quadriceps or patellar tendons or their patellar or tibial insertions</li> <li>2) Tenderness to palpation corresponding to the painful area.</li> <li>3) Presence of a hypoechoic nodular lesion in the patellar tendon on ultrasound imaging.</li> </ol>	138 (19/119)	Students entering an undergraduate program in physical education with 12-14 hours a week of mandatory participation in swimming, track and field, gymnastics, soccer, basketball, volleyball, jazz dance, handball and judo.	18.8 (Range: 17-21)	99/39

Table 2.3 continued.

Cross-sectional Studies						
<b>Bisseling et al. (2007)</b> <sup>133</sup>	BW	<ol style="list-style-type: none"> <li>1) Pain during single-leg decline squat</li> <li>2) Palpation tenderness localized to the proximal patellar tendon or insertion of the quadriceps tendon</li> <li>3) VISA-A score &lt; 80 points</li> </ol>	17 (8/9)	Volleyball players competing in the elite, first, second or third division.	Case: 24.1 (3.3); Control: 23.6 (2.5)	All male
<b>Bode et al. (2007)</b> <sup>134</sup>	BW, Playing surface, Footwear type, Insole use, Activity volume	No specific diagnostic criteria provided.	119 (13/106)	Soccer players competing at the elite level.	15.94 (2.24)	All male
<b>Cassel et al. (2015)</b> <sup>135</sup>	BW, Activity volume	<ol style="list-style-type: none"> <li>1) Positive anamnesis of tendon pain</li> <li>2) Tendon pain on palpation</li> </ol>	760 (42/718)	Athletes enrolled in an elite sport school. Athletes participated in boxing, canoeing, cycling, gymnastics, handball, horse riding, judo, modern pentathlon, rowing, shooting, soccer, swimming, track and field, volleyball, wrestling, recreational sports and weight bearing sports.	13.0 (1.9)	442/318

Table 2.3 continued.

<b>Crossley et al. (2007)*<sup>66</sup></b>	BMI, BW, Peak knee extension torque, Posterior thigh flexibility, Calf muscle endurance, Ankle dorsiflexion ROM, Hop for distance, Six-meter hop test	<ol style="list-style-type: none"> <li>1) Knee pain with either jumping/landing, running or changing directions</li> <li>2) Pain on palpation of the patellar tendon</li> <li>3) VISA-P &lt; 80 points</li> <li>4) Symptoms sufficient to affect exercise and activity for at least 6 months</li> <li>5) Confirmed hypoechoic lesion within the patellar tendon on ultrasonography</li> </ol>	58 (27/31)	Adults participating in competitive basketball, netball, volleyball, soccer or tennis at least once per week.	Unilateral Patellar Tendinopathy : 26 (7); Bilateral Patellar Tendinopathy : 28 (8); Controls: 24 (6)	39/19
<b>Dauty et al. (2007)*<sup>61</sup></b>	BW, Bilateral hamstring and quadriceps peak torque ratios (60, 180, and 240 deg/sec), Bilateral hamstring and quadriceps fatigue ratios	No specific diagnostic criteria provided.	57 (15/42)	Basketball players competing at the elite level.	Case: 25.6 (5); Control: 24.9 (4)	All male
<b>Ferretti et al. (1984)*<sup>118</sup></b>	Playing surface, Activity volume	Clinical diagnosis made by authors, or coach or trainer who was trained and supervised by the primary author during an instructional course. No specific diagnostic criteria provided.	407 (93/314)	Volleyball players from various divisions of the Italian Championship.	Descriptive statistics not stated. 26 athletes < 15, 208 athletes between 15 and 19, 140 athletes between 20 and 25, 33 athletes > 25	Case: 74/19 Control: Not stated

Table 2.3 continued.

<b>Groot et al. (2016)</b> <sup>136</sup>	BMI, Activity volume	<ol style="list-style-type: none"> <li>1) Current symptoms of knee pain in the patellar tendon or its patellar or tibial insertion in connection with training and competitive sports in one knee.</li> <li>2) Symptoms for over three months.</li> <li>3) VISA-P score &lt; 80 points</li> </ol>	44 (22/22)	Recreational athletes	Cases: 27 (10); Controls: 24 (3)	23/21
<b>Krauss et al. (2007)</b> <sup>137</sup>	Running on asphalt, Peak and normalized peak knee extension and flexion concentric and eccentric isokinetic torque (60 deg/sec), Concentric hamstring-quadriceps quotient, Knee flexion and extension eccentric endurance quotient	Presence of at least one of the following: <ol style="list-style-type: none"> <li>1) Pain at the tendon while running, mostly at the inferior pole of the patella.</li> <li>2) Pain after exercise</li> <li>3) Pain generated by contracting the quadriceps muscle</li> <li>4) Well localized tenderness to the inferior pole of the patella</li> </ol>	46 (20/26)	Recreational runners	Cases: 37.6 (8.9); Controls: 39.9 (5.7)	All female
<b>Kujala et al. (1986)</b> <sup>138</sup>	BW, Knee extension ROM, Peak knee flexion and extension isometric torque	<ol style="list-style-type: none"> <li>1) Maximal tenderness on palpation exactly at the lower pole of the patella</li> <li>2) Symptoms at the same point during exertion</li> </ol>	40 (20/20)	Elite and recreational athletes participating in volleyball, long-distance running or orienteering.	Case: 27.4 (6.4); Control: 27.6 (6.0)	All male

Table 2.3 continued.

<b>Lian et al. (1996)</b> <sup>♦139</sup>	BW, Standing jump height (No load, 20-kg load, ½ BW load) and work (No load), CMJ height and work, 15-second rebound test work	<ol style="list-style-type: none"> <li>1) History of pain in the quadriceps or patellar tendons or their patellar or tibial insertions in connection with volleyball play</li> <li>2) Tenderness to palpation corresponding to the painful area</li> </ol>	24 (12/12)	Volleyball players participating in the 1 <sup>st</sup> and 2 <sup>nd</sup> division of the Norwegian Volleyball Federation League.	Case: 23.7 (3.0); Control: 24.8 (4.6)	All male
<b>Lian et al. (2003)</b> <sup>♦140</sup>	BW, Activity volume, Sport specific training volume, Weight training volume, Jump training volume, Stretching habits, Standing jump height (No load, 20-kg load, ½ BW load, 1 BW load) and average work, force and velocity (1/2 and 1 BW load), CMJ height and work, Drop CMJ height and work, 15-second rebound test average work, Jump test composite score	<ol style="list-style-type: none"> <li>1) History of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with volleyball play</li> <li>2) Distinct palpation tenderness corresponding to the painful area</li> </ol>	44 (24/20)	Volleyball players competing at the elite level.	Case: 22.4 (2.5); Control: 22.0 (4.0)	All male
<b>Lian et al. (2005)</b> <sup>♦4</sup>	BW, Activity volume, Weight training volume, Jump training volume	<ol style="list-style-type: none"> <li>1) History of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with athletic activity</li> <li>2) Distinct palpation tenderness corresponding to the painful area</li> </ol>	613 (87/526)	Athletes competing at the national level in soccer, team handball, volleyball, basketball, athletics, ice hockey, wrestling, orienteering or cycling	Mean age ranged from 22.1 to 26.8, depending on sport	506/107

Table 2.3 continued.

<b>Longo et al. (2011)</b> <sup>141</sup>	BW, Impact profile of sport	<ol style="list-style-type: none"> <li>1) Local tenderness to palpation at the inferior pole of the patella or in the main body of the tendon with the knee fully extended and the quadriceps relaxed</li> <li>2) Decreased or eliminated tenderness to palpation when the knee was flexed to 90 degrees</li> </ol>	174 (81/93)	Track and field athletes competing at the elite level.	53.8 (11.4)	103/71
<b>Malliaras et al. (2006)</b> <sup>67</sup>	Ankle dorsiflexion ROM, Sit-and-reach flexibility, Ankle plantarflexion endurance, Activity volume, CMJ height	<ol style="list-style-type: none"> <li>1) Pain elicited during a single-leg decline squat test</li> <li>2) Tendon abnormality on ultrasound imaging.</li> </ol>	140 (53/87) tendons	Volleyball players participating in the Victorian State League competition in Australia.	Right Tendons: 25.8 (4.9); Left Tendons: 26.1 (5.4)	124/66 tendons
<b>Morton et al. (2017)</b> <sup>65</sup>	BMI, Activity volume	Self-report of diagnosis by a medical professional with a positive clinical history and clinical examination, with pain localized to the inferior pole.	825 (193/632)	Recreational to professional athletes competing in volleyball, running, gym exercise, racket sports, basketball, walking/hiking, soccer, cycling, dance/gymnastics/ice skating, field sports, or other sports.	Case: 30.7 (10.8); Control: 30.3 (10.8)	365/460

Table 2.3 continued.

<b>Rio et al. (2016)</b> <sup>♦41</sup>	BMI, Peak knee extension isometric torque, Corticospinal excitability of the quadriceps	<ol style="list-style-type: none"> <li>1) Pain localized to the inferior pole of the patella during jumping and landing activities.</li> <li>2) Pain elicited during the single-leg decline squat test.</li> </ol>	19 (11/8)	Basketball and volleyball players competing at the sub-elite level.	Median (Range): Case: 26 (18-37); Control: 26 (18-37)	Case: 10/1; Control: 7/1
<b>Rosen et al. (2015)</b> <sup>♦142</sup>	Vertical jump height	<ol style="list-style-type: none"> <li>1) Pain only in the patellar tendon</li> <li>2) Self-reported pain within the tendon during loading tasks such as jumping and squatting, during the previous 3 months.</li> <li>3) VISA-P score &lt;80 points</li> </ol>	60 (30/30)	Recreational athletes. Primary sport participation not stated.	Case: 21.3 (3.2); Control: 21.5 (3.0)	Case: 15/15; Control: 15/15
<b>Scattone Silva et al. (2016)</b> <sup>♦143</sup>	BW, Ankle dorsiflexion ROM, Posterior thigh flexibility, Quadriceps flexibility, Activity volume, Peak ankle plantarflexion isometric torque, Peak knee extension isometric torque, Peak hip extension isometric torque	<ol style="list-style-type: none"> <li>1) Pain localized to the patellar tendon of insidious onset, confirmed by palpation.</li> <li>2) Current symptoms in the patellar tendon during tendon-loading task for at least three months</li> </ol>	14 (7/7)	Volleyball, basketball and handball players competing at the college or professional level.	Case: 22.86 (5.43); Control: 21.00 (2.83)	All male
<b>Siegmund et al. (2008)</b> <sup>♦144</sup>	CMJ or running lay-up height	<ol style="list-style-type: none"> <li>1) Diagnosis of bilateral or unilateral jumper's knee by a physician or athletic trainer</li> <li>2) Point tenderness over the inferior pole of the patella on physical examination</li> </ol>	24 (12/12)	Basketball players competing at the recreational, high school, collegiate or professional level.	Not stated. Athletes had to be between the ages of 18 and 29 for inclusion.	All male

Table 2.3 continued.

<b>Torres et al. (2016)</b> <sup>145</sup>	BW	<ol style="list-style-type: none"> <li>1) History of training-related and or competition-related pain in the patellar tendon or its insertions</li> <li>2) Symptoms persisting for more than three months</li> <li>3) Palpation pain and/or tenderness of the patellar tendon</li> <li>4) VISA-P score &lt; 80 points</li> </ol>	42 (21/21)	Basketball and volleyball players. Competition level not stated.	Case: 24.5 (3.6); Control: 25.7 (2.9)	Case: 13/8; Control: 13/8
<b>van der Worp et al. (2011)</b> <sup>8</sup>	Occupational category, Occupational demands	<ol style="list-style-type: none"> <li>1) Self-reported diagnosis of patellar tendinopathy by a physician or physical therapist</li> </ol> <p>OR</p> <ol style="list-style-type: none"> <li>2) Pain at the inferior pole of the patella indicated on a self-administered pain map.</li> </ol>	1505 (268/1237)	Basketball and volleyball players. Competition level not stated.	27.3 (4.1)	690/815
<b>van der Worp et al. (2012)</b> <sup>43</sup>	BW, Waist circumference, Hip circumference, Activity volume, Playing surface	<ol style="list-style-type: none"> <li>1) Self-reported diagnosis of patellar tendinopathy by a physician or physical therapist</li> </ol> <p>OR</p> <ol style="list-style-type: none"> <li>2) Pain at the inferior pole of the patella indicated on a self-administered pain map.</li> </ol>	2224 (414/1810)	Basketball and volleyball players. Competition level not stated.	25.4 (4.7)	1006/1218

Table 2.3 continued.

<p><b>van Wilgen et al. (2013)</b><sup>146</sup></p>	<p>BMI</p>	<ol style="list-style-type: none"> <li>1) History of knee pain in the proximal patellar tendon related to exercise.</li> <li>2) Palpation pain at the proximal patellar tendon.</li> <li>3) Symptoms present for at least 6 months.</li> <li>4) VISA-P score &lt; 80 points.</li> </ol>	<p>32 (12/20)</p>	<p>Athletes participating in basketball, soccer, volleyball, squash or rowing. Competition level not stated.</p>	<p>Case: 23.3 (3.6); Control: 24.7 (5.3)</p>	<p>All male</p>
<p><b>Zhang et al. (2016)</b><sup>59</sup></p>	<p>BMI, BW</p>	<ol style="list-style-type: none"> <li>1) Pain in the inferior pole of patella or the proximal part of the patellar tendon.</li> <li>2) Pain aggravation during single leg squatting and jumping</li> <li>3) Pain duration &gt;3 months.</li> <li>4) Maximum intensity of pain in the previous week &gt;3 on the visual analog scale.</li> <li>5) VISA-P score &lt; 80 points</li> <li>6) Thickening of proximal part of patellar tendon with area of hypoechoic signal on ultrasound imaging.</li> </ol>	<p>66 (36/30)</p>	<p>Volleyball and basketball players. Competition level not stated.</p>	<p>Case: 22.8 (4.2); Control: 23.5 (4.6)</p>	<p>All male</p>

Table 2.3 continued.

<b>Zwerver et al. (2011)*<sup>3</sup></b>	BMI, BW, Activity volume	<ol style="list-style-type: none"> <li>1) Typical history of gradually developed, activity-related anterior knee pain.</li> <li>2) A circumscribed most painful spot, point out in a diagram of the knee, at the upper or lower pole of the patella, in the patellar tendon, or at its tibial insertions.</li> </ol> <p>AND/OR</p> <ol style="list-style-type: none"> <li>3) Diagnosis of patellar tendinopathy by a physician or physical therapist.</li> </ol>	891 (76/815)	Basketball, volleyball, handball, korfbal, soccer, field hockey, or track and field athletes competing at the club and recreational level.	Case: 22.8 (3.1); Control: 24.1 (4.8)	502/389
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BMI = body mass index; BW = bodyweight; ROM = range-of-motion; UCL = Union of European Football Associations (UEFA) Champions League; SWE = Swedish First League; ART = artificial turf cohort; CMJ = counter-movement jump.

\*If a single value is reported, it represents the pooled age for all participants. ♦Study included in quantitative synthesis (meta-analysis).

### **2.4.3 Risk-of-bias assessment**

Prospective studies and cross-sectional studies each had a median NOS score of 5/9 points but there was greater variability in scores for cross-sectional studies (range: 1-8 points) than prospective studies (range: 4-6 points) (Table 2.4). All prospective studies used appropriate selection of a non-exposed cohort (Item 2) and had adequate follow-up (Item 7). One prospective study used independent blind assessment or medical record linkage to determine the presence of patellar tendinopathy (Item 6). All cross-sectional studies used the same method to determine the presence of factors of interest for cases and controls (Item 7) and 23 (92%) used community controls (Item 3). Two cross-sectional studies used secure records or a blinded exam to determine the presence of a factor of interest (Item 6). Inter-rater agreement was almost perfect (Table 2.2). Upon visual inspection, using the Trim and Fill method, there did not appear to be evidence of publication bias for body mass index (BMI), bodyweight or activity volume for cross-sectional studies (Figure 2.3). Other items had too few studies to draw conclusions about publication bias.

Table 2.4: Quality assessment scores on the NOS for included studies.

Author (Year)	Potential Risk Factor or Associated Factor	Covariates Controlled	Selection		Comparability		Exposure/Outcome		Total Stars	Study Quality		
			1	2	3	4	5	6			7	8
<b>Prospective Studies</b>												
de Vries et al. (2015)	All investigated risk factors	Sex, Sport, Playing level	*	*		*	**		*	6	Moderate	
Visnes and Bahr (2013)	Bodyweight, Waist Circumference, Skinfold Measurements	Sex		*	*	*	*		*	*	6	Moderate
Witvrouw et al. (2001)	All investigated risk factors	Sex	*	*	*	*	*		*	6	Moderate	
Backman et al. (2011)	BMI, Bodyweight, Ankle Dorsiflexion ROM			*	*	*			*	*	5	Moderate
Visnes and Bahr (2013)	Volleyball Sets Per Week, Beach Volleyball Training Volume, Strength Training Volume, Jump Training Volume, Other Training Volume	Sex		*		*	*		*	*	5	Moderate
Visnes et al. (2013)	All investigated risk factors	Sex	*		*		*		*	*	5	Moderate
Backman et al. (2011)	Activity Volume, Sport-Specific Training Volume			*		*			*	*	4	Low
Hagglund et al. (2011)	All investigated risk factors			*	*			*	*		4	Low
<b>Cross-Sectional Studies</b>												
Groot et al. (2016)	All investigated factors	Age, Sex	*	*	*	*	**		*	*	8	High

Table 2.4 continued.

<b>Lian et al. (1996)</b>	All investigated factors	Age, Position, Playing Position, Training Volume	*	*	*	*	**	*	*	8	High
<b>Lian et al. (2005)</b>	Weight Training Volume, Jump Training Volume	Age, Height, Weight, Experience at the Elite Level, Training Volume	*	*	*	*	**	*		7	High
<b>Morton et al. (2017)</b>	Activity Volume	Age, Sex	*	*	*		**	*	*	7	High
<b>Rio et al. (2016)</b>	Peak Knee Extension Isometric Torque, Corticospinal Excitability of the Quadriceps	Age, Activity Level	*		*		**	*	*	7	High
<b>Torres et al. (2016)</b>	All investigated factors	Sex, Playing Position	*		*		**	*	*	7	High
<b>Crossley et al. (2007)</b>	All investigated factors	Age, Height	*			*	**	*	*	6	Moderate
<b>Lian et al. (2003)</b>	All investigated factors		*	*	*	*		*	*	6	Moderate
<b>Rio et al. (2016)</b>	BMI	Age, Activity Level	*		*		**	*	*	6	Moderate
<b>Rosen et al. (2015)</b>	All investigated factors	Age, Sex Height, Weight			*	*	**	*	*	6	Moderate

Table 2.4 continued.

<b>Siegmund et al. (2008)</b>	All investigated factors	Height, Weight, Playing Position, Playing Experience, Frequency of Play	*	*	**	*	*	6	Moderate
<b>Zhang et al. (2016)</b>	All investigated factors	Age, Sport	*	*	**	*	*	6	Moderate
<b>Bisseling et al. (2007)</b>	All investigated factors		*	*	*	*	*	5	Moderate
<b>Cassel et al. (2015)</b>	All investigated factors		*	*	*	*	*	5	Moderate
<b>Lian et al. (2005)</b>	Bodyweight, Activity Volume		*	*	*	*	*	5	Moderate
<b>Morton et al. (2017)</b>	BMI		*	*	*	*	*	5	Moderate
<b>Ferretti et al. (1984)</b>	All investigated factors		*	*		*	*	4	Low
<b>Longo et al. (2011)</b>	All investigated factors		*	*		*	*	4	Low
<b>Malliaras et al. (2006)</b>	All investigated factors		*	*		*	*	4	Low
<b>Scattone Silva et al. (2016)</b>	All investigated factors		*	*		*	*	4	Low
<b>Van der Worp et al. (2011)</b>	All investigated factors	Age, Sex		*	**	*		4	Low
<b>Van der Worp et al. (2012)</b>	All investigated factors	Age, Sex, BMI, Sport		*	**	*		4	Low
<b>Van Wilgen et al. (2013)</b>	All investigated factors		*	*		*	*	4	Low
<b>Zwerwer et al. (2011)</b>	All investigated factors			*	*	*	*	4	Low
<b>Bode et al. (2008)</b>	All investigated factors			*		*	*	3	Low

Table 2.4 continued.

<b>Dauty et al. (2007)</b>	All investigated factors	*	*	*	3	Low
<b>Kujala et al. (1986)</b>	All investigated factors	*	*		2	Low
<b>Krauss et al. (2007)</b>	All investigated factors		*		1	Low

‘All investigated (risk) factors’ indicates that the quality assessment scores were identical for all factors of interest included in the study. The cohort version of the NOS was used for prospective studies and the case-control version was used for cross-sectional studies. BMI = body mass index; NOS = Newcastle-Ottawa Scale; ROM = range of motion

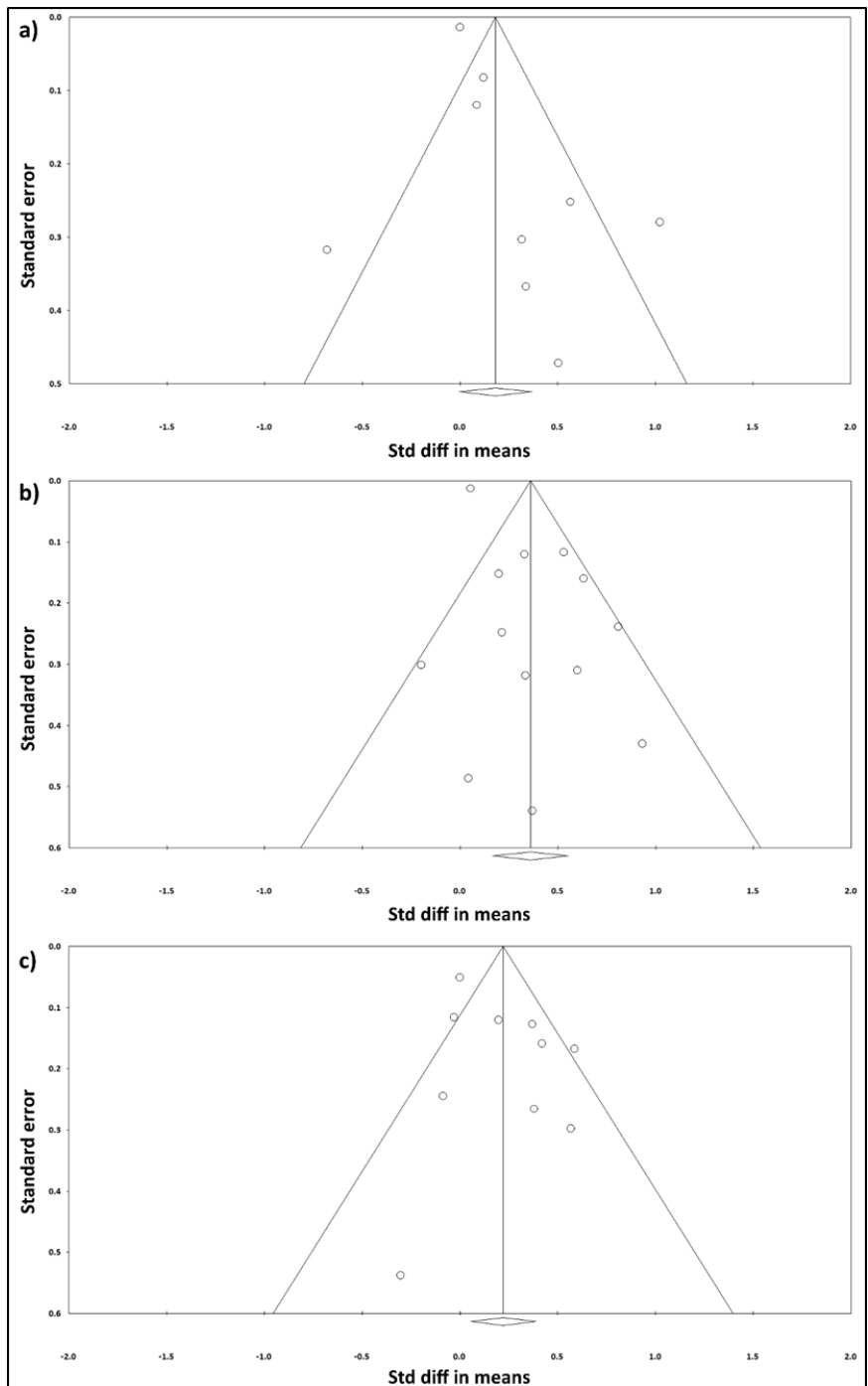


Figure 2.3: Funnel plots for (a) BMI, (b) bodyweight, and (c) activity volume for cross-sectional studies.

## 2.4.4 Prospective studies: Potential risk factors

### 2.4.4.1 Quantitative synthesis: Meta-analysis

#### *Anthropometrics*

Bodyweight was the only prospectively investigated factor appropriate for meta-analysis. Five studies<sup>11,63,111,131,132</sup> with high heterogeneity ( $I^2=55.7$ ) were included. Bodyweight was not significantly associated with risk of patellar tendinopathy ( $p=0.08$ ) (Figure 2.4).

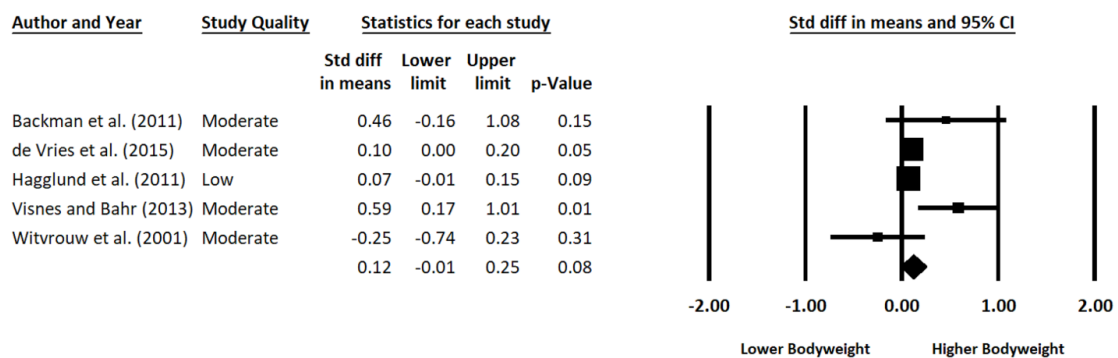


Figure 2.4: Standardized mean difference (Cohen's d) with 95% CI for bodyweight as a potential modifiable risk factor.

### 2.4.4.2 Qualitative synthesis

#### *Joint range-of-motion and muscle length*

Limited evidence from individual moderate quality studies supported decreased ankle dorsiflexion range-of-motion,<sup>131</sup> posterior thigh flexibility,<sup>63</sup> and quadriceps flexibility<sup>63</sup> as potential risk factors (Table 2.5).

Table 2.5: Strength of evidence for potential risk factors (prospective studies) included in qualitative synthesis.

Potential Risk Factor	Study	Study Quality	Positive Findings	Level of Evidence
<b>Anthropometrics</b>				
BMI	Backman et al. (2011)	Moderate	No	No evidence
	de Vries et al. (2015)	Moderate	No	
Waist Circumference	Visnes and Bahr (2013)	Moderate	No	No evidence.
Skin-fold Measures	Visnes and Bahr (2013)	Moderate	No	No evidence.
<b>Joint Range-of-Motion and Muscle Length</b>				
Ankle dorsiflexion ROM	Backman et al. (2011)	Moderate	Yes	Limited evidence for decreased ankle dorsiflexion ROM.
Posterior Thigh Flexibility	Witvrouw et al. (2001)	Moderate	Yes	Limited evidence for decreased posterior thigh flexibility
Quadriceps Flexibility	Witvrouw et al. (2001)	Moderate	Yes	Limited evidence for decreased quadriceps flexibility.
<b>Sports and Activity Related Factors</b>				
Activity Volume	de Vries et al. (2015)	Moderate	No	Conflicting evidence for increased activity volume.
	Visnes et al. (2013)	Moderate	Yes	
	Backman et al. (2011)	Low	No	
	Hagglund et al. (2011)	Low	Yes	
Strength Training Volume	Visnes and Bahr (2013)	Moderate	No	No evidence.
Jump Training Volume	Visnes and Bahr (2013)	Moderate	Yes	Limited evidence for greater volume of jump training per week.
Sport Surface	de Vries et al. (2015)	Moderate	No	No evidence.
	Hagglund et al. (2011)	Low	No	
Sport Specific Training Volume	Backman et al. (2011)	Low	No	No evidence.

Volleyball Sets Played Per Week	Visnes and Bahr (2013)	Moderate	Yes	Limited evidence for greater number of volleyball sets played per week.
Beach Volleyball Training Volume	Visnes and Bahr (2013)	Moderate	No	No evidence.
Training Volume in Sports Other Than Primary Sport (Volleyball or Basketball)	de Vries et al. (2015) Visnes and Bahr (2013)	Moderate	No	No evidence.
Training/Match Exposure Ratio	Hagglund et al. (2011)	Low	No	No evidence
<b>Functional Testing</b>				
CMJ Height	Visnes et al. (2013)	Moderate	Yes	Limited evidence for greater CMJ height in men. No evidence in women.
Standing Jump Height	Visnes et al. (2013)	Moderate	No	No evidence.
<b>Muscle Performance</b>				
Knee Extension Torque	Witvrouw et al. (2001)	Moderate	No	No evidence.
Knee Flexion Torque	Witvrouw et al. (2001)	Moderate	No	No evidence.
<b>Occupational Demands</b>				
Occupational Classification	de Vries et al. (2015)	Moderate	No	No evidence.
Knee Loading During Work	de Vries et al. (2015)	Moderate	No	No evidence.

BMI = body mass index; ROM = range-of-motion; CMJ = counter-movement jump

### *Sports and activity related factors*

Limited evidence from one moderate quality study supported greater volume of jump training and greater number of volleyball sets played per week as potential risk factors.<sup>68</sup> There was conflicting evidence from four moderate to low quality studies for increased activity volume as a potential risk factor (Table 2.5).<sup>11,111,131,132</sup>

### *Functional testing*

There was limited evidence from one moderate quality study supporting greater counter-movement jump height as a potential risk factor in male athletes (Table 2.5).<sup>111</sup>

## **2.4.5 Cross-sectional studies: Associated modifiable factors**

### **2.4.5.1 Quantitative synthesis: Meta-analysis**

#### *Anthropometrics*

BMI and bodyweight were appropriate for meta-analysis. For BMI, nine studies with high heterogeneity ( $I^2=71.7$ ) were included in the meta-analysis (Figure 2.5).<sup>3,41,43,59,65,66,136,145,146</sup> BMI was not significantly associated with patellar tendinopathy ( $p=0.06$ ) (Figure 2.5). One low quality study<sup>3</sup> was excluded from the meta-analysis due to insufficient data but the reported results were in agreement with the quantitative synthesis. For bodyweight, 13 studies with high heterogeneity ( $I^2=77.8$ ) were included in the meta-analysis (Figure 2.5).<sup>3,4,141,143,59,61,66,132,133,135,138,140</sup> There was a small, positive effect for bodyweight, indicating that greater bodyweight is significantly associated with patellar tendinopathy (Figure 2.5). This effect translates to an odds ratio of 1.92 (95% CI: 1.35 to 2.73). One low quality study was

excluded due to insufficient data.<sup>134</sup> In this study, weight did not differ significantly between young elite soccer players with or without patellar tendinopathy.

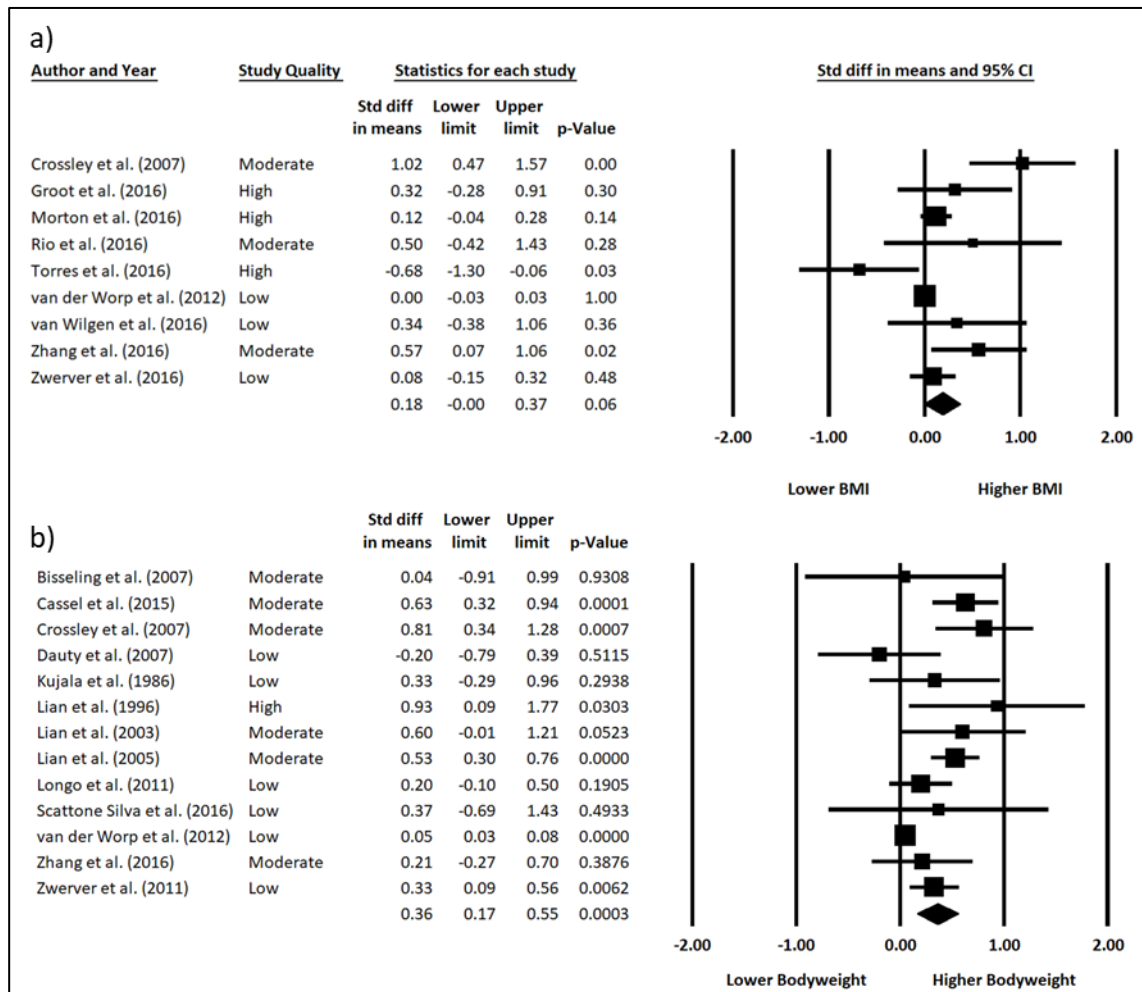


Figure 2.5: Standardized mean differences (Cohen's d) with 95% CI for (a) BMI and (b) bodyweight as associated modifiable factors.

### *Sport and activity related factors*

Activity volume was appropriate for meta-analysis. Ten studies with high heterogeneity ( $I^2=67.0$ ) were included (Figure 2.6).<sup>3,4,43,65–67,118,135,140,143</sup> There was a small, positive effect for activity volume, indicating that greater activity volume is significantly associated with patellar tendinopathy (Figure 2.6). This effect translates to an odds ratio of 1.50 (95% CI: 1.11 to 2.02). Two low quality studies and one high quality study were excluded due to insufficient data. These studies did not find a significant association between hours of weekly sports participation<sup>3</sup> or training<sup>134,136</sup> and patellar tendinopathy.

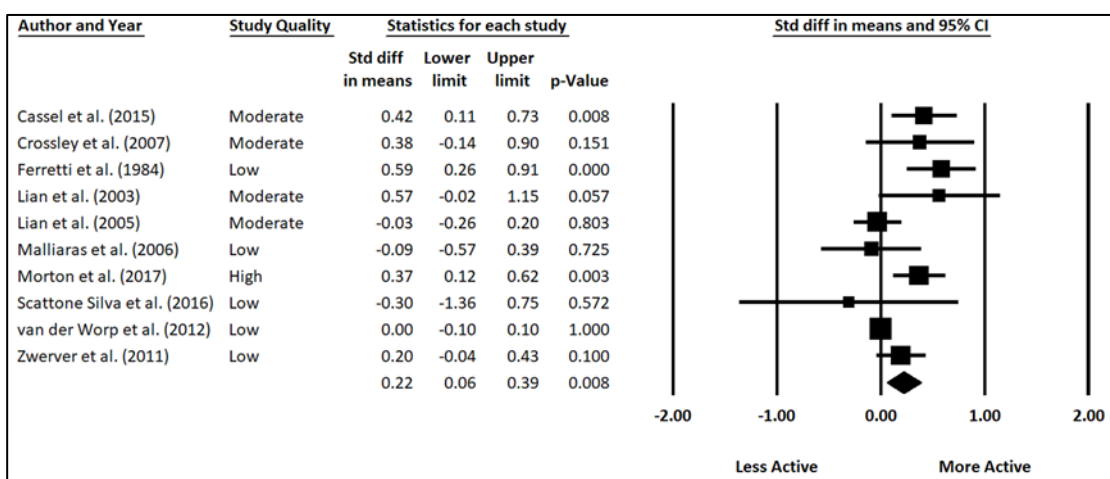


Figure 2.6: Standardized mean difference (Cohen's d) with 95% CI for activity volume as an associated modifiable factor.

### *Functional testing*

Counter-movement jump (CMJ) height was appropriate for meta-analysis. The CMJ height included performance on the CMJ, drop CMJ and vertical jump, as these

measures allow a counter movement and assess an athlete’s ability to utilize the stretch-shortening cycle.<sup>147</sup> Five studies with moderate heterogeneity ( $I^2=44.2$ ) were included (Figure 2.7).<sup>67,139,140,142,144</sup> There was a small, positive effect for CMJ height, indicating that greater CMJ height is associated with patellar tendinopathy (Figure 2.7). This effect translates to an odds ratio of 1.77 (95% CI: 1.13 to 2.77).

*Muscle performance*

Knee extension torque production was appropriate for meta-analysis. Five studies with high heterogeneity ( $I^2=89.7$ ) were included (Figure 2.7).<sup>41,61,137,138,143</sup> Knee extension torque production was not significantly associated with patellar tendinopathy ( $p=0.19$ ) (Figure 2.7).

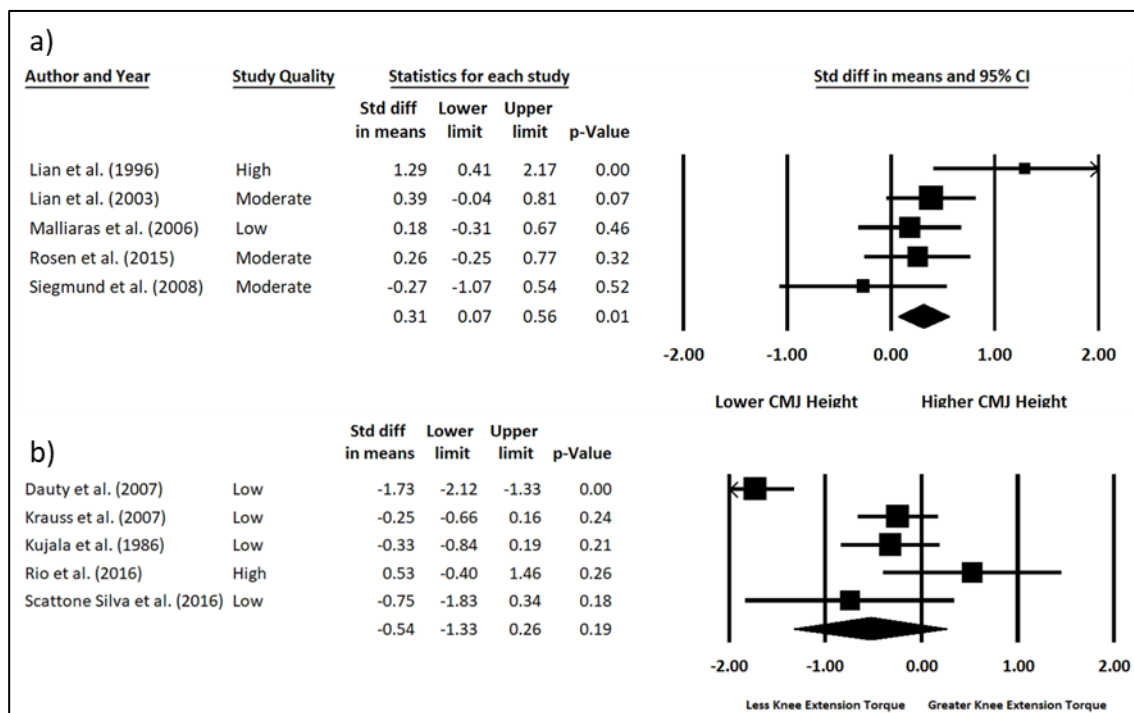


Figure 2.7: Standardized mean differences (Cohen’s d) with 95% CI for (a) CMJ height and (b) knee extension torque production as associated modifiable factors.

#### **2.4.5.2 Qualitative synthesis**

##### *Joint range-of-motion and muscle length*

There was conflicting evidence from three moderate to low quality studies for decreased ankle dorsiflexion range-of-motion and altered posterior thigh flexibility as associated modifiable factors (Table 2.6).<sup>66,67,143</sup>

Table 2.6: Strength of evidence for associated modifiable factors (cross-sectional studies) included in qualitative synthesis.

Associated Modifiable Factor	Study	Study Quality	Positive Findings	Level of Evidence
<b>Anthropometrics</b>				
Waist Circumference	Van der Worp et al. (2012)	Low	No	No evidence.
Hip Circumference	Van der Worp et al. (2012)	Low	No	No evidence.
Waist-to-hip Ratio	Van der Worp et al. (2012)	Low	No	No evidence.
<b>Joint Range-of-Motion and Muscle Length</b>				
Ankle Dorsiflexion ROM	Crosley et al. (2007)	Moderate	No	Conflicting evidence for decreased ankle dorsiflexion ROM.
	Malliaras et al. (2006)	Low	Yes	
	Scattone Silva et al. (2016)	Low	Yes	
Posterior Thigh Flexibility	Crosley et al. (2007)	Moderate	Yes	Conflicting evidence for both increased and decreased posterior thigh flexibility.
	Malliaras et al. (2006)	Low	No	
	Scattone Silva et al. (2016)	Low	Yes	
Quadriceps Flexibility	Scattone Silva et al. (2016)	Low	No	No evidence.
Knee Extension ROM	Kujala et al. (1986)	Low	No	No evidence.
<b>Sports and Activity Related Factors</b>				
Strength Training Volume	Lian et al. (2005)	High	Yes	Moderate evidence for greater volume of strength training per week.
	Lian et al. (2003)	Moderate	Yes	

Table 2.6 continued.

Jump Training Volume	Lian et al. (2005)	High	No	Conflicting evidence for greater volume of jump training per week.
	Lian et al. (2003)	Moderate	Yes	
Sport Surface	Bode et al. (2017)	Low	No	No evidence.
	Ferretti et al. (1984)	Low	Not Tested	
	Krauss et al. (2007)	Low	No	
	van der Worp et al. (2012)	Low	No	
Running Workouts per Week	Krauss et al. (2007)	Low	No	No evidence.
Weekly Running Mileage	Krauss et al. (2007)	Low	No	No evidence.
Running Speed	Krauss et al. (2007)	Low	Yes	Limited evidence for running at a slower average pace.
Impact Profile of Sport	Longo et al. (2011)	Low	No	No evidence.
Sport Specific Training Volume	Lian et al. (2003)	Moderate	No	No evidence.
Quantity of Stretching Before or After Training	Lian et al. (2003)	Moderate	No	No evidence.
Shoe Type	Bode et al. (2017)	Low	No	No evidence.
Insole Use	Bode et al. (2017)	Low	No	No evidence.
<b>Functional Testing</b>				
Standing Jump Height	Lian et al. (1996)	High	Yes	Conflicting evidence for greater standing jump height with a 20-kg load. No evidence for greater jump height without an external load or with a ½ BW load.
	Lian et al. (2003)	Moderate	No	
Standing Jump Work	Lian et al. (1996)	High	Yes	Conflicting evidence for greater work performed during the standing jump.
	Lian et al. (2003)	Moderate	No	
Average Force during Standing Jump	Lian et al. (2003)	Moderate	Yes	Limited evidence for greater average force during a standing jump with a ½-BW or a 1-BW load.
Average Power During Standing Jump	Lian et al. (2003)	Moderate	Yes	Limited evidence for greater average power during a standing jump with a ½-BW or a 1-BW load.
Average Velocity During Standing Jump	Lian et al. (2003)	Moderate	No	No evidence.

Table 2.6 continued.

CMJ Work	Lian et al. (1996)	High	Yes	Conflicting evidence for greater CMJ work.
	Lian et al. (2003)	Moderate	No	
Drop CMJ Work	Lian et al. (2003)	Moderate	Yes	Limited evidence for greater drop CMJ work from a 45 cm height.
CMJ-Standing Jump Height	Lian et al. (1996)	High	Yes	Conflicting evidence for greater CMJ-standing jump height.
	Lian et al. (2003)	Moderate	No	
Average Power on 15-Second Rebound Test	Lian et al. (1996)	High	Yes	Conflicting evidence for greater average power on the 15-second rebound.
	Lian et al. (2003)	Moderate	No	
Jump Test Composite Score	Lian et al. (2003)	Moderate	Yes	Limited evidence for better performance on a battery of jump tests.
6-Meter Hop Test Time	Crossley et al. (2007)	Moderate	No	No evidence.
Hop for Distance	Crossley et al. (2007)	Moderate	No	No evidence.
<b>Muscle Performance</b>				
Knee Flexion Torque	Dauty et al. (2007)	Low	No	No evidence.
	Krauss et al. (2007)	Low	No	
	Kujala et al. (1986)	Low	No	
Plantarflexion Endurance	Crossley et al. (2007)	Moderate	No	No evidence.
	Malliaras et al. (2006)	Low	No	
Normalized Peak Plantarflexion Torque	Scattone Silva et al. (2016)	Low	No	No evidence.
Knee Extension Fatigue Ratio	Dauty et al. (2007)	Low	Yes	Limited evidence for decreased knee extension fatigue ratio.
Knee Flexion Fatigue Ratio	Dauty et al. (2007)	Low	No	No evidence.
Knee Extension Eccentric Endurance Quotient	Krauss et al. (2007)	Low	Not Tested	No evidence.
Knee Flexion Eccentric Endurance Quotient	Krauss et al. (2007)	Low	Not Tested	No evidence.
Concentric Hamstring to Quadriceps Quotient	Krauss et al. (2007)	Low	No	No evidence.

Table 2.6 continued.

Normalized Peak Hip Extension Torque	Scattone Silva et al. (2016)	Low	Yes	Limited evidence for decreased normalized hip extension torque.
Stimulus Response Curve for the Motor Evoked Potential of the Quadriceps	Rio et al. (2016)	High	Yes	Moderate evidence for a steeper slope to the motor evoked potential curve for the quadriceps.
<b>Occupational Demands</b>				
Occupational Classification	van der Worp et al. (2011)	Low	Yes	Limited evidence for heavy physically demanding work.
Knee Loading During Work	van der Worp et al. (2011)	Low	No	No evidence.

ROM = range-of-motion; BW = bodyweight; CMJ = counter-movement jump.

### *Sport and activity related factors*

Moderate evidence from one high and one moderate quality study supported greater volume of strength training per week as an associated modifiable factor (Table 2.6).<sup>4,140</sup> Limited evidence from one low quality study supported slower average running pace as an associated modifiable factor (Table 2.6).<sup>137</sup> There was conflicting evidence from one high and one moderate quality study for greater volume of jump training per week as associated modifiable factors (Table 2.6).<sup>4,140</sup>

### *Functional testing*

Limited evidence from one moderate quality study supported greater average force and power with a ½- or 1-bodyweight load during a standing jump, greater work performed during a drop CMJ, and better performance on a jump test battery as associated modifiable factors (Table 2.6).<sup>140</sup> There was conflicting evidence from one high quality and one moderate quality study for greater standing jump height with a 20-kg load, work performed during a standing jump or CMJ, difference between CMJ and standing jump height, and average power on 15-second rebound test as associated modifiable factors (Table 2.6).<sup>139,140</sup>

### *Muscle performance*

Moderate evidence from one high quality study supported a steeper slope for the motor evoked potential curve of the quadriceps, representing altered corticospinal excitability to the quadriceps, as an associated modifiable factor (Table 2.6).<sup>41</sup> Limited evidence from individual low quality studies supported decreased knee extension fatigue ratio<sup>61</sup> and normalized peak hip extension torque<sup>143</sup> as associated modifiable factors (Table 2.6).

### *Occupational demands*

Limited evidence from one low quality study supported heavy physically demanding work as an associated modifiable factor (Table 2.6).<sup>8</sup>

## **2.5 Discussion**

### **2.5.1 Main findings**

There is a lack of strong evidence for any prospectively investigated potential modifiable risk factors for patellar tendinopathy. However, there was limited or conflicting evidence that decreased ankle dorsiflexion range-of-motion, decreased posterior thigh and quadriceps flexibility, greater volume of jump training, more volleyball sets played per week, greater CMJ height, and greater activity volume are potential modifiable risk factors for patellar tendinopathy. Additionally, there was a lack of strong evidence for any associated modifiable factor reported in cross-sectional studies. Moderate to conflicting evidence supported greater volume of strength training, better jumping performance, less normalized hip extension torque, decreased knee extension fatigue ratio, and altered corticospinal excitability to the quadriceps as associated modifiable factors.

### **2.5.2 Risk-of-bias and study quality**

In agreement with the findings of van der Worp et al., there were few prospective studies investigating risks factors and none were high quality.<sup>44</sup> Many of the cross-sectional studies were low quality and nearly half failed to control for covariates, which limits the strength of evidence for associated modifiable factors. However, there was no evidence of publication bias in the meta-analysis of BMI,

bodyweight or activity volume in cross-sectional studies. In light of these findings, additional high-quality, prospective studies are needed.

### **2.5.3 Anthropometric measures**

A systematic review by Gaida et al.<sup>148</sup> found that adiposity, including the surrogate measures of BMI and body weight, is frequently associated with tendinopathy and may be a risk factor for tendon injuries. In contrast, this study found no evidence supporting anthropometric measures as potential risk factors for patellar tendinopathy. Although a small, positive effect was found for bodyweight in cross-sectional studies, suggesting that greater bodyweight is an associated modifiable factor, bodyweight was not significantly associated with an increased risk of patellar tendinopathy in prospective studies. Patellar tendinopathy is most common in young athletic individuals<sup>3</sup> and the majority of studies included in this review were conducted in elite athletes. Therefore, it is unlikely that the athletes in these studies had high adiposity. Instead, higher body weight likely reflects a taller stature and a build that is more muscular.<sup>149</sup>

### **2.5.4 Joint range-of-motion and muscle length**

Individual moderate quality prospective studies identified decreased ankle dorsiflexion range-of-motion, posterior thigh flexibility and quadriceps flexibility as potential risk factors for patellar tendinopathy. In one prospective and one cross-sectional study, athletes had a higher risk of patellar tendinopathy if their dorsiflexion range-of-motion fell below cut-off scores of 36.5°<sup>131</sup> or 45.0°,<sup>67</sup> respectively. When jumping, adequate ankle joint range-of-motion is of importance since the ankle is responsible for absorbing 37% to 50% of the total kinetic energy during the landing

phase.<sup>150</sup> Additionally, decreased dorsiflexion is moderately correlated with higher ground reaction forces during a drop landing task.<sup>151</sup> This increase in ground reaction force, coupled with potentially altered ability to absorb kinetic energy at the ankle, may increase patellar tendon loads. Furthermore, decreased ankle weight-bearing dorsiflexion range-of-motion results in altered knee kinematics during squatting,<sup>152</sup> which may increase patellar tendon loads during athletic activities.<sup>122</sup> It is hypothesized that decreased posterior thigh flexibility may contribute to patellar tendon overload by decreasing the mechanical advantage of the extensor mechanism and increasing the demands placed on the quadriceps during knee extension.<sup>143</sup> Similarly, decreased quadriceps flexibility may contribute to overload by increasing passive tension within the patellar tendon.<sup>59</sup> Based on the limited evidence, clinicians may want to assess for restrictions in these measures but further research using high quality, prospective study designs is warranted.

### **2.5.5 Sport and activity related factors**

Patellar tendinopathy is considered an overuse injury so an association between higher levels of activity or training and injury is expected.<sup>153</sup> Therefore, the limited or conflicting evidence from prospective studies regarding volume of activity or jump training and the small effect from cross-sectional studies for activity volume is surprising. This may be explained in part by the composition of the studies and how activity was defined. The plurality of studies consisted of elite athletes so the participants are likely completing a high volume of training and there is minimal variability between groups. Additionally, activity was typically reported as a duration, with no indication of the intensity, type of activity, or whether activity level had changed. Activity duration alone may not accurately describe the load-placed on the

patellar tendon or the tendon's readiness to accommodate those loads. Thus, future studies should examine patellar tendon load during activity and the relationship between current and previous level of activity to provide a more complete picture of how activity contributes to patellar tendinopathy. Although there was no evidence from the sole prospective study investigating weekly strength training volume, there was moderate evidence from two cross-sectional studies that greater weekly strength training volume may be an associated modifiable factor. In designing prevention or rehabilitation programs, clinicians may want to consider altering the volume of activity, jump or strength training to reduce cumulative tendon load. Additionally, other parameters, such as intensity, activity type and prior activity level, and their relationship to recovery should be considered.

#### **2.5.6 Functional testing**

Although greater CMJ height is the only measure with prospective support, limited or conflicting evidence identified higher values on other metrics of jump performance as associated modifiable factors. This suggests that athletes with greater jumping ability are at higher risk of developing patellar tendinopathy. With greater jumping ability, athletes are likely generating greater forces at take-off<sup>154</sup> and must dissipate greater vertical ground reaction forces at landing.<sup>155</sup> As a result, they experience a higher cumulative load on the extensor apparatus for a given jump. These athletes may also be completing a higher quantity or frequency of jumps since they likely have more opportunities to play and are more involved while on the court. A recent systematic review of the relationship between jump biomechanics and patellar tendinopathy identified a "stiff" landing pattern as a potential risk factor for patellar tendinopathy.<sup>122</sup> The authors also emphasized that adequate lower extremity flexibility

and range-of-motion are necessary to utilize a more flexible landing pattern, which may be protective against patellar tendinopathy. Since better jumping ability is desirable in an athletic population, clinicians should consider modifying landing biomechanics and lower extremity flexibility and range-of-motion instead to reduce the risk of injury.

### **2.5.7 Muscle performance**

There was no evidence from prospective studies or a meta-analysis of cross-sectional studies that knee extension torque production was associated with patellar tendinopathy. However, there was moderate to limited evidence from individual cross-sectional study that altered corticospinal excitability to the quadriceps and decreased knee extension fatigue ratio may be an associated modifiable factor. This suggests that quadriceps muscle performance may be altered in patellar tendinopathy but this alteration may not be captured by torque production alone. Participation in jumping sports requires rapid force development, high levels of lower extremity power, and multi-joint coordination.<sup>156</sup> Additionally, these muscle performance tests are typically performed in a rested state and do not assess how these measures may change with fatigue. It should be noted that knee extension torque was the only muscle performance measure relating to the quadriceps that was prospectively investigated. Thus, further research is warranted to determine if other measures of quadriceps muscle performance, such as fatigue resistance, endurance, power and muscle activation, are related to the development of patellar tendinopathy.

There was also limited evidence supporting decreased normalized hip extension torque as an associated modifiable factor. During landing tasks, the hip extensors are responsible for dissipating 20 to 25% of the kinetic energy absorbed by

the lower extremities.<sup>150</sup> Therefore, decreased hip extensor strength may increase demands placed on the knee extensors. Furthermore, the contribution of the hip extensors to energy dissipation increases when utilizing a softer landing strategy.<sup>150,157</sup> To compensate for decreased hip extension strength, individuals may adopt a stiffer landing strategy, which has been previously identified as a potential risk factor for patellar tendinopathy.<sup>122</sup> Clinicians may want to assess for hip extension strength deficits in prevention programs, although prospective studies are needed to confirm if this deficit is a risk factor for patellar tendinopathy.

### **2.5.8 Occupational demands**

There was no prospective evidence that occupational classification (e.g. heavy vs. light physically demanding work) is a potential risk factor for patellar tendinopathy. However, there was limited evidence from one cross-sectional study that heavy physically demanding work may be an associated modifiable factor. Given the limited evidence and lack of prospective support, it is unlikely that occupational classification is a risk factor for patellar tendinopathy.

### **2.5.9 Patellar tendinopathy and tendon load**

Patellar tendinopathy is considered an overuse injury resulting from repetitive stress to the patellar tendon with insufficient recovery.<sup>112</sup> This is supported by the findings of this systematic review and meta-analysis, as each of the potential modifiable risk factors with support from prospective studies may directly or indirectly increase the loads placed on the patellar tendon. However, some of these risk factors, such as jumping ability, may be beneficial to athletic performance and undesirable to change. Therefore, clinicians may need to manipulate other training

parameters to reduce the cumulative load on the tendon or increase recovery time between activities.

#### **2.5.10 Limitations**

There were several limitations to our review. First, different versions of the NOS were used for prospective and cross-sectional studies. Therefore, quality assessment ratings are not comparable between study designs. Although certain cross-sectional studies scored higher than prospective studies, the cross-sectional studies are not able to establish a temporal relationship between the factor of interest and patellar tendinopathy. Second, included studies encompassed a variety of populations, methods and research questions, which is reflected in the high heterogeneity between studies. A consequence of high heterogeneity is that the calculated effect may be due to the differences in study design or populations evaluated, not true differences in the outcome of interest.<sup>127</sup> To address this limitation, a random-effects model was used when heterogeneity was high, as this provides a more conservative estimate of the effect size. Third, many potential risk factors or associated factors were investigated by a limited number of studies and many of these, especially for cross-sectional studies, had small sample sizes. This limits the strength of evidence for these items and lack of support does not indicate that an item of interest is definitely not associated with patellar tendinopathy. Therefore, clinicians should use their clinical judgement and not completely disregard other potential risk factors when creating an individualized prevention program. Fourth, a large portion of these studies were conducted in male, elite athletes. Although this is representative of the population most commonly diagnosed with patellar tendinopathy, it may limit generalizability to female and recreational athletes. Finally, there was large variability between

definitions of patellar tendinopathy, which was expected, as the definition of patellar tendinopathy has shifted over time. However, this potentially introduces bias by incorporating individuals with other diagnosis. Despite this concern, the decision was made to include broader definitions of patellar tendinopathy, as the prevalence of other diagnosis is typically low compared to true patellar tendinopathy and we did not want to exclude a large body of previous research.<sup>118</sup>

## **2.6 Conclusions**

There was limited or conflicting evidence that decreased ankle dorsiflexion range-of-motion, decreased posterior thigh and quadriceps flexibility, greater volume of jump training, more volleyball sets played per week, greater CMJ height, and greater activity volume are potential modifiable risk factors for patellar tendinopathy. However, this evidence is based on few moderate or low-quality prospective studies.

## Chapter 3

### RELIABILITY AND STABILITY OF cSWE AT THE PATELLAR TENDON IN PATIENTS WITH PATELLAR TENDINOPATHY

#### 3.1 Introduction

The patellar tendon runs from the inferior pole of the patella to the tibial tuberosity and is a critical link in the extensor mechanism of the knee, facilitating force transmission from the quadriceps muscles to the lower leg.<sup>46</sup> It is comprised of densely packed collagen fibrils surrounded by a ground substance, consisting primarily of proteoglycans and water.<sup>158</sup> The collagen fibrils are oriented along the long axis of the tendon and are dominated by Type I collagen, which gives the tendon its tensile strength.<sup>159</sup> The patellar tendon is viscoelastic, meaning their deformation is dependent on the rate of loading.<sup>158,160</sup> At high loading rates the tendon will appear stiffer and deform less than at lower loading rates, when the load remains the same.<sup>158,160</sup> These structural and mechanical characteristic allows for rapid force transmission during high velocity, ballistic movements, such as jumping. However, due to the high demands placed on the patellar tendon, it is very susceptible to injury, especially in repetitive jumping sports such as basketball and volleyball.<sup>3,4</sup>

Patellar tendinopathy is a clinical diagnosis of load-dependent pain and stiffness in the patellar tendon, most commonly seen in jumping athletes.<sup>1-4</sup> This injury is also accompanied by changes in tendon morphology<sup>30-34</sup> and mechanical properties.<sup>35-40</sup> The initial, recommended treatment for patellar tendinopathy is exercise therapy, which consists of patellar tendon loading exercises.<sup>13,14</sup> The aim of

this treatment is to promote tendon remodeling, restore mechanical function and reduce symptoms.<sup>16,17,42,18–25</sup>

Appropriate load prescription is a critical component of successful exercise therapy for patellar tendinopathy. Loads must be adequate to promote remodeling<sup>84</sup> without excessive overload, which results in further degeneration and worsening of symptoms.<sup>85–87</sup> Determining the optimal load for a tendon is challenging since we have lacked responsive measures of tendon health. Traditionally, pain has been the primary guide for load prescription.<sup>21,27</sup> However, clinical improvements in symptoms do not correlate with changes in tendon structure.<sup>83</sup> Thus, pain should not be used as a surrogate measure of tendon remodeling. Alternatively, B-mode ultrasound imaging has been used to assess changes in tendon structure and as a marker of remodeling.<sup>89</sup> However, these changes occur slowly so they have limited utility in measuring a tendon's short-term response to a bout or bouts of loading.<sup>20,89,90</sup>

Mechanical properties have been proposed as a more responsive measure of tendon health and remodeling, which may provide clinicians with the ability to tailor loads to individual patients during exercises therapy.<sup>91,92</sup> There are two principle methods for non-invasive evaluation of tendon mechanical properties, B-mode ultrasound imaging synchronized with mechanical dynamometry<sup>38</sup> and elastography.<sup>161</sup> B-mode ultrasound imaging synchronized with mechanical dynamometry has been used to measure tensile stiffness and Young's modulus.<sup>38</sup> However, this technique is reliant on muscle contraction, which is altered in the presence of pain.<sup>97</sup> Therefore, this method may not be appropriate for injured populations. More recently, several forms of commercial elastography scanners have been used to quantify tendon stiffness.<sup>107,162–165</sup> Elastography is a form of ultrasound

imaging which measures a tissues response to an applied mechanical perturbation and does not rely on muscle contraction.<sup>166</sup>

There are two primary commercial forms of elastography used to assess tendon mechanical properties, strain elastography and shear wave elastography.<sup>167</sup> In strain elastography, a stress is applied perpendicular to the long axis of the tendon via compression with the ultrasound transducer and the perpendicular strain is recorded.<sup>167</sup> The strain is used to generate color maps, or elastograms, of relative tissue stiffness.<sup>167</sup> Additionally, these elastograms may be used to calculate a strain ratio or index, comparing the tissue of interest to a reference tissue.<sup>168</sup> The utility of this method is limited, since it only provides qualitative values or relative stiffness and does not provide true estimates of mechanical properties. In shear wave elastography, shear waves are generated parallel or perpendicular to the tissue of interest, typically by an acoustic radiation force, and the velocity of the shear wave is recorded.<sup>167</sup> The shear wave speed can be used to create elastograms and calculate shear elastic modulus or dynamic shear modulus.<sup>167</sup> However, commercial systems utilize a burst of unspecified acoustic frequencies, which limits the precision with which they may estimate mechanical properties.<sup>91</sup> Furthermore, this method often lacks the measurement range necessary for relatively stiff tendon.<sup>98,99</sup> As a result, the elastograms become saturated and underestimate tendon mechanical properties.

Our research group has developed an alternative method of elastography, called continuous shear wave elastography (cSWE), which overcomes the limitations of commercial scanners and provides additional measures of tissue mechanics.<sup>91</sup> Briefly, a mechanical perturbation is applied using an external actuator at eleven set frequencies and the resultant linear displacement of the tendon is recorded by a high

frequency ultrasound probe, centered over the tissue of interest.<sup>91</sup> The raw radiofrequency data is utilized to calculate shear wave speed and estimate static shear modulus and viscosity.<sup>91</sup> Shear modulus is obtainable by commercial scanners but the ability to quantify viscosity is unique to cSWE. This method has been validated against magnetic resonance elastography<sup>91</sup> and shown to be reliable for measuring Achilles tendon mechanical properties.<sup>92,169</sup> In pilot studies, we have adapted this method to the patellar tendon and shown that it has the sensitivity to detect differences in mechanical properties between healthy and injured patellar tendons. Prior to investigating this method's utility in guiding load prescription, it is critical to understand its reliability and stability at the patellar tendon in individuals with patellar tendinopathy, which has not been evaluated.

Therefore, the purpose of this study is to establish stability and reliability of cSWE to evaluate the mechanical properties of the patellar tendon in individuals with patellar tendinopathy and examine the standard error of the measure and smallest detectable change of these properties.

## **3.2 Methods**

### **3.2.1 Study Design**

This study was performed over two sessions, approximately 24 hours apart, and consisted of two parts – within-session reliability and between-session stability. Individuals with patellar tendinopathy were recruited. A standardized clinical exam was performed by a licensed physical therapist to ensure that participants had the diagnosis of interest and met inclusion/exclusion criteria. To be included, participants had to be at least 18 years old and be diagnosed with patellar tendinopathy in the past

three months. The diagnostic criteria for patellar tendinopathy was 1) pain and stiffness localized to the patellar tendon and 2) load-dependent symptoms, which increased as demands placed on the patellar tendon increased.<sup>2,170</sup> Participants were excluded if they were unwilling to refrain from physical activity, beyond what is necessary for daily activities and work, prior to the first testing session or between sessions. This study was approved by the University of Delaware Institutional Review Board and all participants received written and oral information regarding the study and provided informed consent prior to participation.

At the baseline session, participants height, weight, past medical history, and symptom severity were recorded. A standardized B-mode ultrasound examination of the tendon was performed by an experience musculoskeletal ultrasonographer to assess tendon morphology. Continuous shear wave elastography (cSWE) was performed once for each limb by an experienced examiner (Examiner 1) with four years of experience using this method. At the end of the session, all skin markings were removed and the participants were asked to refrain from physical activity prior to the next session.

At the second session (24-hours later), cSWE was performed three times for each limb. The first two assessments were completed by Examiner 1 and the third assessment was completed by a second, novice examiner (Examiner 2). Examiner 2 received two hours of training in identifying appropriate landmarks, positioning the participant, and applying the ultrasound probe prior to study initiation. They had no prior experience with ultrasound imaging. Between each assessment, all skin markings were removed by an individual that would not be performing the method. The

landmarks were then identified and marked, and the probe was repositioned by the examiner performing the assessment.

### **3.2.2 Past Medical History**

Participants completed online questionnaires via Research Electronic Data Capture (REDCap)<sup>171,172</sup> hosted at the University of Delaware to record their duration of patellar tendon symptoms, affected limb, and history of lower extremity injuries, including Osgood-Schlatter disease, and Sinding-Larsen Johansson syndrome. Additionally, their history of surgery and injections to the patellar tendon were recorded.

### **3.2.3 Symptom Severity**

Symptom severity was assessed by palpation and the Victorian Institute of Sport Assessment – Patellar tendon (VISA-P) questionnaire.<sup>6,173</sup> For palpation, the participant was positioned in supine with 30° of knee flexion and their knee supported by a bolster. The patellar tendon was palpated along its entire length and participants were asked to rate their palpatory pain on the numeric pain rating scale (0-10, 0 = no pain, 10 = worst pain imaginable).<sup>174,175</sup> The VISA-P is a patient reported outcome measure designed to evaluate severity of patellar tendon symptoms.<sup>6,173</sup> Scores range from 0 to 100, which lower scores indicating a greater degree of symptoms.

### **3.2.4 Tendon Morphology**

Patellar tendon morphology was assessed by B-mode ultrasound imaging using a LOGIC *e* Ultrasound (GE Healthcare, Chicago, IL) system using a wide-band linear array probe (5.0 – 13.0 MHz). The subject was positioned in supine with knees flexed to 30° and supported by a bolster, in accordance with European Society of

Musculoskeletal Radiology guidelines.<sup>176</sup> Three long-axis extended-field-of-view and three short-axis images were taken 1 cm distal to the inferior patellar pole to evaluate tendon thickness and cross-sectional. A custom MATLAB code was used to identify maximal tendon thickness and Osirix MD imaging software (Pixmeo, Geneva, Switzerland) was used to measure cross-sectional area.<sup>177,178</sup> The average of three measurements was used for analysis of thickness and cross-sectional area.

### **3.2.5 Continuous Shear Wave Elastography (cSWE)**

Continuous shear wave elastography (cSWE) was used to assess patellar tendon mechanical properties using a SonixMDP Q+ (Ultrasonix, Vancouver, BC, Canada) ultrasound scanner with an L14-5/38 probe.<sup>91,169</sup> For this method, the participant was seated on an adjustable plinth at 90° of hip and knee flexion, with the back supported. The lower legs were stabilized using walking boots attached to a weighted platform to reduce muscular contraction and movement artifact (Figure 3.1). Once positioned, the inferior pole of the patella and the tibial tuberosity were identified and marked. An additional marking was placed 1 cm distal to the inferior pole of the patella, along the imaginary line connecting the inferior pole and the tibial tuberosity. The ultrasound transducer was clamped in an adjustable 3-prong clamp and centered over the 1 cm mark, aligned with the long axis of the tendon. For each trial, a Minshaker Type 4810 (Bruel and Kjaer, Norcross, GA, USA) was placed on the quadriceps tendon, just proximal to the superior pole of the patella to produce shear waves at 11 ascending excitation frequencies (322, 339, 358, 379, 402, 429, 460, 495, 536, 585, 643 Hz). During each frequency, raw radiofrequency data was captured by the ultrasound probe at a framerate of 6438 frames/sec. Three trials were performed per limb. Between trials the ultrasound probe was lifted and re-applied to ensure

adequate contact and that it had not shifted from the region of interest. Using a custom MATLAB code, static shear modulus and viscosity were calculated on a pixelwise basis, as described by Cortes et al and Corrigan et al, to obtain values of static shear modulus and viscosity.<sup>91,169</sup> The previously described processing method was altered to include 11 frequencies, rather than 6, due to an increase in processing power and reduction in time burden. Inclusion of all 11 frequencies should provide a more precise estimate of patellar tendon mechanical properties. All processing was completed by the same examiner (Examiner 1), who was blinded to the participant, trial and limb. The average of three trials was used for analysis.



Figure 3.1: Participant positioning and set-up for cSWE.

### 3.2.6 Data Analysis

Data analysis was performed using RStudio version 1.2.5033.<sup>179,180</sup> Descriptive statistics were calculated for participant demographics. Within-session reliability and

between-session stability were examined using intra-class correlation coefficients (ICC) and reported as ICC (95% confidence interval) for static shear modulus and viscosity.<sup>181</sup> Reliability and stability were examined separately for the most and least symptomatic limb. If participants had unilateral symptoms then the injured limb was assigned as the most symptomatic. In instances of bilateral symptoms, the limb with the lower VISA-P score was assigned as the most symptomatic limb. ICC values are interpreted based on guidelines established by Koo & Li, where values less than 0.5 indicate poor reliability, between 0.5 and 0.75 indicate moderate reliability, between 0.75 and 0.9 indicate good reliability, and greater than 0.9 indicate excellent reliability.<sup>181</sup> The standard error of the measure (SEM) and smallest detectable change (SDC) were calculated and reported in the unit of measure for each mechanical property, based on values obtained for between-days stability.<sup>182</sup>

### **3.2.6.1 Reliability**

Intra-rater reliability was examined using a mean-rating, absolute-agreement, two-way mixed effects model (ICC<sub>3,3</sub>) comparing values obtained for trials two and three (Figure 2).<sup>181</sup> Inter-rater reliability was examined using a mean-rating, absolute-agreement two-way random effects model (ICC<sub>2,3</sub>) comparing values obtained for trials three and four (Figure 3.2).<sup>181</sup>

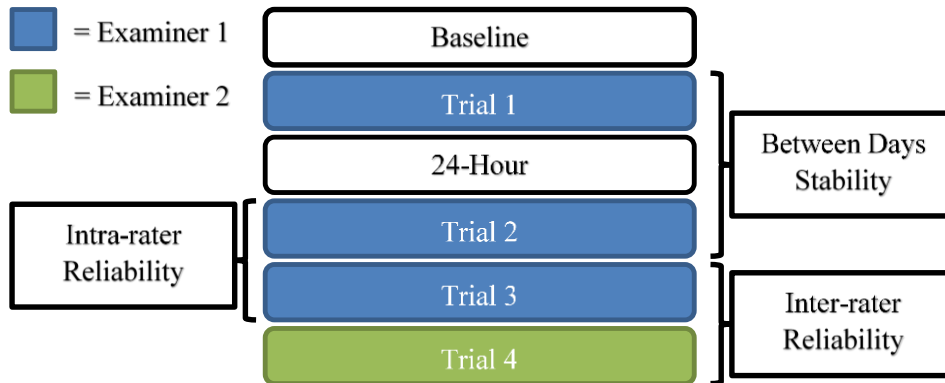


Figure 3.2: Study design for evaluating intra-rater reliability, inter-rater reliability, and between days stability.

### 3.2.6.2 Stability

Between days stability was examined using a mean-rating, absolute-agreement, two-way mixed effects model (ICC<sub>3,3</sub>), comparing values obtained for trials one and two obtained by the experienced examiner 1 (Figure 3.2).<sup>181</sup>

## 3.3 Results

### 3.3.1 Participants

Thirteen participants (4 female) with a mean (SD) age of 31.2 (9.4) years, height of 178.5 (11.3) cm, and weight of 78.0 (17.0) kg were recruited for this study. One participant had symptoms in the right limb, 9 had symptoms in the left limb, and 3 had bilateral symptoms. Of those with bilateral symptoms, the most symptomatic side was the right for 1 participant and the left for 2 participants. Three participants had a history of Osgood-Schlatter disease in their left limb. One participant had their right patellar tendon harvested for an anterior cruciate ligament graft, which was the same side as their patellar tendon symptoms. None of the participants had a history of

Sinding-Larsen Johansson syndrome, injection to the patellar tendon, or other surgery to the patellar tendon.

### **3.3.2 Symptom Severity**

The median (min-max) palpatory pain in the most symptomatic limb was 1 (0-6) points. The mean (SD) score on the VISA-P questionnaire was 80.5 (14.6) points.

### **3.3.3 Tendon Morphology**

The mean (SD) tendon thickness was 6.4 (1.6) mm for the most symptomatic limb and 6.0 (1.0) for the least symptomatic limb. The mean (SD) tendon cross-sectional area was 11.7 (2.8) mm<sup>2</sup> for the most symptomatic limb and 12.1 (3.2) mm<sup>2</sup> for the least symptomatic limb.

### **3.3.4 Reliability**

The mean (SD) static shear modulus and viscosity for each limb and trial are listed in table 3.1. Static shear modulus had moderate intra-rater reliability for the most and least symptomatic limbs, with ICCs of 0.664 (0.097 – 0.875) and 0.742 (0.306 – 0.904), respectively. Viscosity had good intra-rater reliability for the most and least symptomatic limbs, with ICCs of 0.874 (0.662 – 0.953) and 0.877 (0.669 – 0.954), respectively. Inter-rater reliability of static shear modulus was poor for the most symptomatic limb, with an ICC of 0.220 (-0.795 – 0.691), and moderate for the least symptomatic limb, with an ICC of 0.682 (0.169 – 0.881). Inter-rater reliability of viscosity was moderate for the most symptomatic limb, with an ICC of 0.733 (0.304 – 0.900), and good for the least symptomatic limb, with an ICC of 0.872 (0.667 – 0.952).

### **3.3.5 Stability**

Static shear modulus had good between-days stability for the most and least symptomatic limbs, with ICCs of 0.610 (-0.047 – 0.885) and 0.564 (-0.172 – 0.838), respectively. Between-days stability of viscosity was excellent for the most symptomatic limb, with an ICC of 0.933 (0.819 – 0.975), and good for the least symptomatic limb, with an ICC of 0.760 (0.356 – 0.911). The SEM and SDC values are listed in table 3.2.

Table 3.1: Mechanical properties measured by cSWE for each limb and trial.

Symptomatic Limb	Trial 1		Trial 2		Trial 3		Trial 4	
	Most	Least	Most	Least	Most	Least	Most	Least
<b>Static Shear Modulus (kPa) mean (SD)</b>	76.5 (24.7)	78.1 (34.0)	80.3 (16.4)	77.5 (20.9)	74.1 (28.0)	76.2 (16.4)	60.0 (19.7)	79.0 (25.6)
<b>Viscosity (Pa*s) mean (SD)</b>	29.4 (10.5)	30.4 (11.8)	31.3 (10.5)	30.1 (10.3)	26.8 (11.2)	31.4 (12.3)	25.2 (9.9)	31.0 (9.5)

Table 3.2: Standard error of the measure (SEM) and smallest detectable change (SDC) values for mechanical properties of each limb.

Symptomatic Limb	SEM		SDC <sub>95%-individual</sub>		SDC <sub>95%-group</sub>	
	Most	Least	Most	Least	Most	Least
<b>Static Shear Modulus (kPa)</b>	14.1	21.1	39.1	58.6	10.8	16.3
<b>Viscosity (Pa*s)</b>	1.4	4.9	3.8	13.6	1.1	3.8

### **3.4 Discussion**

We found moderate intra-rater reliability for static shear modulus and good intra-rater reliability for viscosity. Inter-rater reliability for static shear modulus was poor-to-moderate and moderate-to-good for viscosity. Additionally, between-days stability was good for static shear modulus and good-to-excellent for viscosity. However, caution should be used when interpreting these values since 95% confidence intervals around the estimates were relatively large for both mechanical properties, which may reflect the small sample size. SEM and SDC change values for static shear modulus were relatively large. Conversely, SEM and SDC change values for viscosity were relatively small. Based on these findings, it appears that viscosity is a more reliable and stable measure than static shear modulus when measured by cSWE.

The relatively lower inter-rater reliability for static shear modulus and viscosity is likely due to the limited experience by Examiner 2. This suggests that to utilize cSWE a person may require further training or more experience with ultrasound imaging to obtain proficiency. However, until the effect of additional training and experience is examined, cSWE for patellar tendinopathy should be performed by the same experienced examiner when evaluating changes in mechanical properties within individuals or making comparisons between individuals.

#### **3.4.1 Comparison to cSWE at the Achilles tendon**

Intra-rater reliability and stability of mechanical properties for the Achilles tendon have previously been evaluated using nearly identical methods by Corrigan *et al.*<sup>169</sup> In comparison to the values obtained for the Achilles tendon, cSWE at the patellar tendon has comparable or higher ICCs for static shear modulus and viscosity.<sup>169</sup> The

SEM and SDC values are higher for static shear modulus and comparable or lower for viscosity at the patellar tendon, when compared to the Achilles tendon.<sup>169</sup> However, it should be noted that values obtained for the Achilles tendon were from a healthy population without structural changes. Furthermore, stability measures were based on multiple sessions, over four hours, rather than between-days, which may explain the larger SEM and SDC values obtained for static shear modulus at the patellar tendon.

### **3.4.2 Comparison to other forms of elastography**

Numerous studies have reported the reliability and stability of mechanical properties of the patellar tendon using commercially available elastography systems.<sup>36,109,189–192,163,168,183–188</sup> However, only two of these studies have utilized these methods in an injured population.<sup>183,192</sup> Akkaya et al. reported intra- and inter-rater reliability of strain elastography in individuals after bone-patellar tendon-bone graft harvest and Zardi et al. reported intra-rater reliability of shear wave elastography in individuals with orthopedic injuries that did not involve the patellar tendon.<sup>183,192</sup> Therefore, this is the first study to report reliability and stability of an elastography method in individuals with patellar tendinopathy.

In prior studies, the reported reliability and stability measures have varied widely, likely due to differences in the method of measurement, system used, parameters reported, measurement location, participant positioning, examiner experience, and study design (Table 3.3).<sup>36,109,189–192,163,168,183–188</sup> This makes comparison of the values obtained in this study to prior work challenging. Furthermore, since prior studies have not reported static shear modulus or viscosity, it is not possible to directly compare SEM or SDC values. ICCs for the strain ratio or strain index measured by strain elastography range from 0.13 to 0.96 for intra-rater

reliability and from 0.0 to 0.98 for inter-rater reliability (Table 3.3).<sup>168,183–186</sup> Between-days stability has not been reported for strain elastography of the patellar tendon.<sup>168,183–186</sup> ICCs for the shear wave velocity, dynamic shear modulus or shear elastic modulus measured by shear wave elastography range from 0.23 to 1.00 for intra-rater reliability and 0.71 to 0.97 for inter-rater reliability (Table 3.3).<sup>109,163,187–192</sup> ICCs for between-days stability range from 0.63 to 0.83 (Table 3.3).<sup>36109163</sup> Additionally, one study had to exclude individuals due to saturation of the elastograms, indicating that the system did not have the measurement range to evaluate stiffer tendons.<sup>189</sup> Overall, ICCs for intra-rater reliability, inter-rater reliability and stability of static shear modulus obtained in this study were below the upper limit of the majority of values reported for strain and shear wave elastography. However, ICCs for intra- and inter-rater reliability of viscosity were comparable or only slightly below the upper limit of the majority of the values reported for strain and shear wave elastography. Furthermore, ICCs for between-days stability were comparable or higher.

Table 3.3: Intra-rater reliability, inter-rater reliability, and between days stability for elastography of the patellar tendon reported in prior studies.

Author, Year	Ultrasound System	Population	Parameters Reported	Intra-rater Reliability	Inter-rater Reliability	Between-days Stability
<b>Strain Elastography</b>						
Ağladioğlu et al., 2016 <sup>168</sup>	LOGIQ E9 (GE Medical Systems, Wauwatosa, WI, USA)	69 adult smokers and non-smokers (12 female)	Strain ratio	Proximal: 0.858 Middle: 0.930 Distal: 0.797		
Akkaya et al., 2016 <sup>183</sup>	LOGIQ E9 (GE Medical Systems, Wauwatosa, WI, USA)	18 adults (1 female) with bone-patellar tendon-bone graft harvest	Strain ratio	Proximal: 0.809 – 0.892 Middle: 0.932 – 0.964 Distal: 0.814 – 0.844	Proximal: 0.927 Middle: 0.982 Distal: 0.946	
Dickson et al., 2019 <sup>184</sup>	LOGIQ S8 (GE Medical Systems, Wauwatosa, WI, USA)	20 healthy adults	Strain index, Strain ratio	Strain index: 0.17 – 0.72 Strain ratio: 0.13 – 0.91	Strain index: 0.0 – 0.57 Strain ratio: 0.0 – 0.54	
Dickson et al., 2020 <sup>185</sup>	LOGIQ S8 (GE Medical Systems, Wauwatosa, WI, USA); MyLab 70 XVG (Esaote, Genoa, Italy)	20 healthy adults (15 female)	Strain ratio	Proximal: 0.40 – 0.85 Middle: 0.13 – 0.67 Distal: 0.15 – 0.91		
Porta et al., 2014 <sup>186</sup>	MyLab70 Gold XV (Esaote, Genoa, Italy)	11 healthy, young adults (7 female)	Strain ratio	Proximal: 0.749 – 0.790 Middle: 0.654 – 0.740 Distal: 0.666 – 0.705	Proximal: 0.644 Middle: 0.597 Distal: 0.527	

Table 3.3 continued.

Shear Wave Elastography						
Coombes et al., 2018a <sup>187</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	6 healthy, young adults	Shear wave velocity	Anterior: 0.92 Posterior: 0.93		
Coombes et al., 2018b <sup>36</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	6 healthy adults	Shear wave velocity			Middle: 0.71 Proximal: 0.80
Fontenelle et al., 2018 <sup>188</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	18 healthy, young adult males	Dynamic shear modulus	0° of knee flexion: 0.856 80° of knee flexion: 0.998		
Hsiao et al., 2015 <sup>189</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	5 healthy, young adults	Shear elastic modulus	Proximal: 0.831-0.874 Middle: 0.966 – 0.991 Distal: 0.835 – 0.878	Proximal: 0.742 Middle: 0.821 Distal: 0.783	
Mannarino et al., 2018 <sup>109</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	22 healthy, young, adult males	Shear elastic modulus	Dominant limb: 0.886 – 0.928 Non-dominant limb: 0.888 – 0.900		Dominant limb: 0.651 Non-dominant limb: 0.630
Peltz et al., 2013 <sup>190</sup>	Aixplorer (Supersonic Imaging, Aix-en-Provence, France)	12 healthy adults (6 female)	Shear elastic modulus	Right limb: 0.23 – 0.74 Left limb: 0.40 – 0.90		
Taş et al., 2017 <sup>163</sup>	Acuson S3000 (Siemens Medical Solutions, Mountain View, CA, USA)	12 healthy males	Shear wave velocity	0.91 – 0.92	0.71	0.81-0.83

Table 3.3 continued.

Zhang & Fu, 2013 <sup>191</sup>	Aixplorer (Supersonic Imaging, Aix-en- Provence, France)	11 healthy, young adults (3 female)	Shear elastic modulus	0.98	0.97
Zardi et al., 2019 <sup>192</sup>	MyLab Nine (Esaote, Genoa, Italy)	18 adults (9 female) referred for an orthopedic condition not involving the patellar tendon	Shear elastic modulus	0.989	

### 3.4.3 Limitations

This study has several limitations. First, there was a small sample size, which partially explains the wide confidence intervals surrounding the ICC estimates. Second, cSWE was only performed at the proximal portion of the patellar tendon. This location was chosen since the proximal patellar tendon is the most common site of patellar tendon pathology.<sup>118</sup> However, it is possible for symptoms to occur anywhere along the length of the tendon and it is unclear whether reliability and stability would be similar at other locations along the tendon.<sup>118</sup> Five previous studies have reported intra- or inter-rater reliability of elastography at the proximal, middle and distal third of the patellar tendon.<sup>168,183,185,186,189</sup> Four of these studies found that reliability was higher in the middle third, compared to the proximal and distal third,<sup>168,183,185,189</sup> while one study found reliability to be highest at the proximal third.<sup>186</sup> Finally, although cSWE overcomes some of the problems of commercial elastography systems, it is not without limitations. cSWE utilizes the Voight model to calculate static shear modulus and viscosity, which assumes a linear isotropic material under no stress.<sup>91,193</sup> The patellar tendon is a nonlinear, anisotropic structure. However, when deformations are small, which is the case with cSWE, the effect of nonlinearity is negligible. Additionally, anisotropic materials have a proportional relationship between the square of the wave speed and shear modulus when the wave is traveling along one of the main anisotropy axes, which is similar to the relationship observed for isotropic materials. Furthermore, shear wave speed is influenced by tensile stress and tendon thickness but there is not currently a method for that accounts for all of these effects. To limit the effect of tensile stress, participant positioning was standardized at 90° of

hip and knee flexion and they were stabilized in walking boots to limit muscular contraction.

### **3.5 Conclusions**

cSWE has adequate intra-rater reliability and stability to evaluate static shear modulus and viscosity of the patellar tendon in individuals with patellar tendinopathy. However, measurements should be made by the same experienced examiner when making comparison within or between individuals or groups. Compared to commercial elastography systems, this method may provide additional biomarkers of injury and recovery, which may be of interest in individualizing loads during exercise therapy for patellar tendinopathy. However, further studies are needed to determine how sensitive cSWE is to changes indicative of tendon remodeling.

## Chapter 4

### EXPLORATION OF RELATIONSHIPS BETWEEN TENDON STRUCTURE AND CONSTITUENTS OF TENDON HEALTH IN PATELLAR TENDINOPATHY

#### 4.1 Introduction

The cardinal symptom of patellar tendinopathy is load-dependent patellar tendon pain.<sup>1,2</sup> However, patellar tendinopathy is also accompanied by changes in other domains of tendon health. Individuals with patellar tendinopathy have decreased lower extremity function,<sup>5-8</sup> impaired muscle performance,<sup>41,42</sup> and altered tendon structure.<sup>30,31,40,32-39</sup> Tendon structure can be further subdivided into two categories, morphology and mechanical properties. Altered morphology, or tendinosis, is typically assessed using B-mode ultrasound imaging and is characterized by localized tendon thickening, irregular fiber alignment and hypoechoic regions.<sup>31,57</sup> Mechanical properties describe how the tendon responds when loaded. There is no consensus on the direction of change for mechanical properties as a result of patellar tendinopathy, which is likely due to variability in the methods of measurement, the parameters reported, and the patient's phase in the injury process.<sup>39</sup> Yet, overwhelmingly, the current evidence suggests that mechanical properties are altered in patellar tendinopathy.<sup>35-40</sup>

The clinical relevance of tendon structural changes in patients with patellar tendinopathy has been extensively debated.<sup>83,102,194</sup> Those that argue that structural changes are of little clinical importance do so based on several reasons. First,

morphological changes are common in active individuals<sup>195</sup> and up to 79% of those with abnormalities do not develop symptoms at short- or long-term follow-ups.<sup>102</sup> Second, symptoms typically resolve prior to changes in morphology or mechanical properties.<sup>19,20</sup> Third, there is not a clear relationship between clinical improvements and normalization of tendon structure.<sup>83</sup> However, the treatment with the highest level of evidence for patellar tendinopathy is exercise therapy.<sup>13,14</sup> The mechanism of action for exercise therapy is mechanotransduction, or the process by which forces applied to the tendon trigger cellular responses that result in structural remodeling.<sup>15</sup> So, those that argue against the clinical importance of structural changes typically utilize treatment protocols that are designed to address alterations in tendon structure.

The importance of tendon structure is clear in other tendon injuries, namely the Achilles tendon. Chang & Kulig demonstrated that alteration in Achilles tendon morphology and mechanical properties, in the absence of symptoms, contribute to changes in motor system control, resulting in reduced triceps surae activity and functional performance.<sup>29</sup> Therefore, alterations in Achilles tendon structure influence other domains of tendon health. Several studies have attempted to examine whether similar relationships exist between patellar tendon structure and other domains of tendon health.<sup>25,35,107–110,40,41,101–106</sup> However, the presence of such relationships, their strength and/or direction varies between studies so the importance of alterations in patellar tendon structure remains unclear.<sup>25,35,40,107–109</sup>

An improved understanding of the relationship between patellar tendon structure and other components of tendon health may help explain the presence of clinical impairments, such as decreased lower extremity function and quadriceps muscle performance. Additionally, this may result in more targeted treatments, which aim to

resolve these impairments by addressing the contribution of altered tendon structure. Therefore, the purpose of this study is to explore the relationships between patellar tendon structure and symptom severity, lower extremity function, and quadriceps muscle performance in individuals with unilateral patellar tendinopathy.

## **4.2 Methods**

### **4.2.1 Study Design**

This study is a cross-sectional, retrospective analysis of individuals that participated in one of two previous studies of patellar tendinopathy. These studies were approved by the University of Delaware Institutional Review Board. Prior to study enrollment, participants received written and oral information about study participation and provided written informed consent. To be included in the analysis, participants had to have a clinical diagnosis of patellar tendinopathy. The diagnostic criteria for patellar tendinopathy was 1) pain and stiffness localized to the patellar tendon and 2) load-dependent symptoms, which increased as demands placed on the patellar tendon increased.<sup>2,170</sup> The baseline evaluation was used for each participant, where age, sex, BMI, tendon structure, symptom severity, lower extremity function and quadriceps muscle performance were recorded. Additionally, individuals' values for tendon structure were excluded if the participant had an invasive procedure to the patellar tendon that may alter tendon structure, such as a patellar tendon graft harvest. Furthermore, values for lower extremity function and quadriceps muscle performance were excluded if participants had another injury that may influence their test results.

## 4.2.2 Tendon Structure

### 4.2.2.1 Morphology

Patellar tendon morphology was assessed by B-mode ultrasound imaging using a LOGIC *e* Ultrasound (GE Healthcare, Chicago, IL) system with a wide-band linear array probe (5.0 – 13.0 MHz). The participant was positioned in supine with knees flexed to 30° and supported by a bolster, in accordance with European Society of MusculoSkeletal Radiology guidelines.<sup>176</sup> Three extended-field-of-view long axis images were taken from the tibial tuberosity to the inferior pole of the patella and three short axis images were taken 1 cm distal to the inferior pole of the patella. A custom MATLAB program was used to obtain maximal tendon thickness from long axis images. (Figure 4.1). Short axis images were used to measure cross-sectional area (CSA) using Osirix MD imaging software (Pixmeo, Geneva, Switzerland) (Figure 4.2). The mean value of three images was used for data analysis.

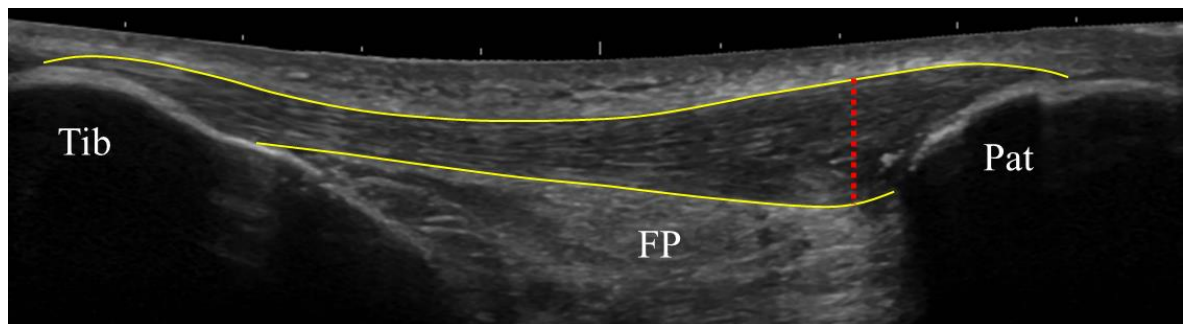


Figure 4.1: Extended-field-of-view long-axis image of the patellar tendon with maximal thickness measure (red dashed line). The borders of the patellar tendon are outline in yellow. Tib = Tibial tuberosity; Pat = patella; FP = Hoffa's fat pad.

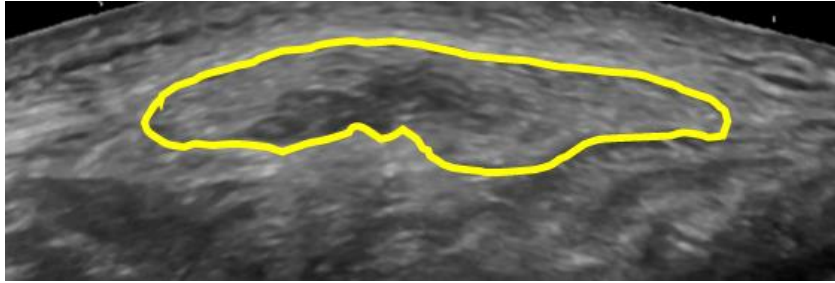


Figure 4.2: Short axis image of the patellar tendon with cross-sectional area measure (yellow line).

#### 4.2.2.2 Mechanical Properties

Tendon mechanical properties were evaluated using continuous shear wave elastography (cSWE) to obtain values of static shear modulus and viscosity. cSWE was performed using a SonixMDP Q+ (Ultrasonix, Vancouver, BC, Canada) ultrasound scanner with an L14-5/38 probe.<sup>91,169</sup> Participants were seated on an adjustable plinth at 90° of hip and knee flexion, with the back supported and lower legs stabilized. Skin markings were placed 1 cm distal to the inferior pole of the patella, along the imaginary line connecting the inferior pole and the tibial tuberosity. The ultrasound transducer was positioned over the 1 cm mark, aligned with the long axis of the tendon and clamped in an adjustable 3-prong clamp. Shear waves were generated at 11 ascending frequencies (322, 339, 358, 379, 402, 420, 460, 495, 536, 585, 643 Hz) using a Minishaker Type 4810 (Bruel and Kjaer, Norcross, GA, USA) placed on the quadriceps tendon. The resultant linear displacement of the tendon was recorded by the ultrasound probe at a framerate of 6438 frames/sec. Three trials were performed per limb and a custom MATLAB code was used in post-processing to obtain mechanical properties, as described by Cortes et al and Corrigan et al.<sup>91,169</sup> The average of three trials was used for data analysis.

### **4.2.3 Symptom Severity**

Symptom severity was assessed using the Victorian Institute of Sport Assessment – Patellar Tendon (VISA-P) questionnaire.<sup>6,173</sup> The VISA-P is a patient reported outcome measure designed to assess symptom severity in individuals with patellar tendinopathy. Scores ranges from 0 to 100 with lower scores indicating more severe symptoms.

### **4.2.4 Lower Extremity Function**

Lower extremity function was evaluated using the counter-movement jump (CMJ) and drop CMJ tests.<sup>196</sup> For the CMJ, participants began on flat ground, standing on a single-leg with their arms behind their back (Figure 4.3). After familiarization with procedures, they were instructed to quickly bend their leg and then jump as high as possible, landing on the same leg. For the drop CMJ, participants assumed the same starting position as the CMJ on a 20 cm high box (Figure 4.3). They were instructed to “drop” or “fall” off of the box and then to immediately jump as high as possible after contacting the ground, landing on the same leg. For both tests, three trials were performed per limb and participants were asked to rate their pain during the activity on the numeric pain rating scale (NPRS) (0 = no pain, 10 = worst pain imaginable).<sup>175</sup> Flight time was recorded for each trial using a light mat (MuscleLab®, Ergotest Innovations, Stathelle, Norway) and was used to estimate jump height. The average of three trials for each limb was used for data analysis.

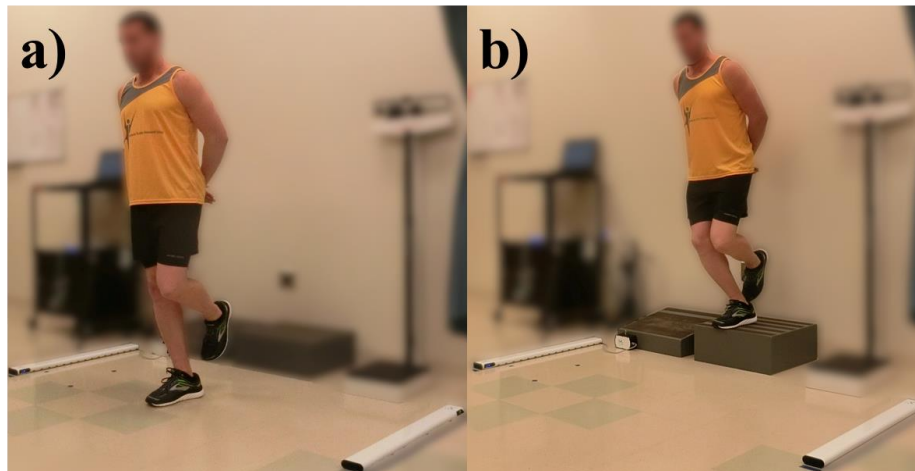


Figure 4.3: Starting position for the (a) CMJ and (b) drop CMJ.

#### 4.2.5 Quadriceps Muscle Performance

Knee extension strength and quadriceps muscle activation were assessed using the burst-superimposition technique on a Biodex Systems 3 dynamometer (Shirley, NY).<sup>197</sup> Participants were positioned in 90° of hip flexion and 60° of knee flexion. Self-adhesive electrodes were placed over the vastus medialis and vastus lateralis muscle bellies (Figure 4.4). After a standardized warm-up and familiarization with procedures, the participants performed a 5-second maximum voluntary isometric contraction (MVIC). During the MVIC, a supramaximal, 10-pulse (600  $\mu$ s, 130 V, 100 pulses per second) train of electrical stimulation was delivered to the muscle using an electrical stimulator (Grass Technologies, Champaign, IL). If the participant was unable to activate the quadriceps fully, testing was repeated up to 4 times, with 3 minutes rest between trials. The maximal voluntary force and the force attributable to the electrical stimulation was recorded (Figure 4.4). After each trial, participants were asked to rate their pain on the NPRS. The best trial, based on force production and visual inspection of the force production graph, was selected to calculate quadriceps

central activation ratios ( $CAR = [MVIC \text{ force} / \text{burst augmented force}] \times 100\%$ ) (Figure 4.4). The CAR is a measure of quadriceps inhibition, where lower values indicate a greater degree of quadriceps inhibition.

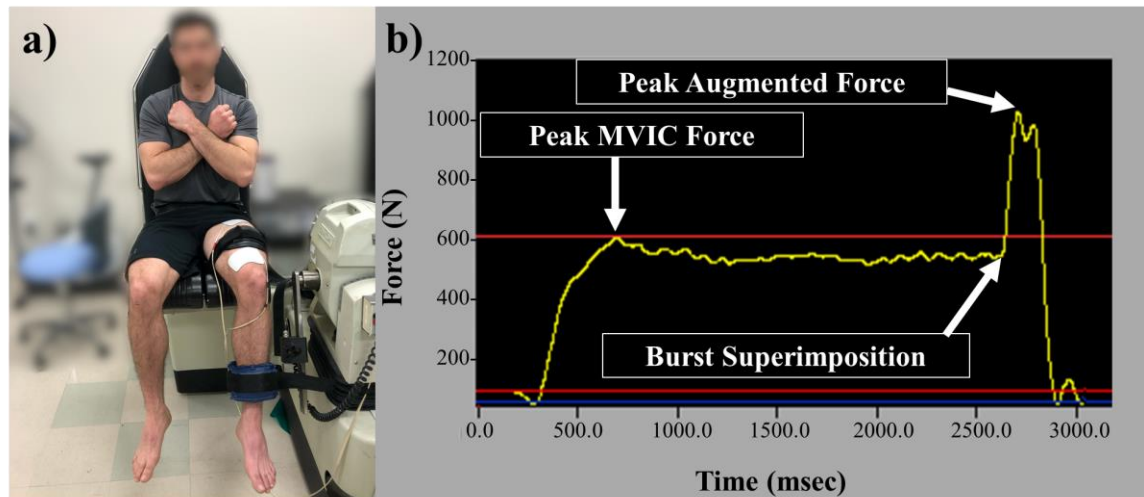


Figure 4.4: (a) Set-up for knee extension strength and activation testing. (b) Force production trace with increase in force at onset of burst superimposition, characteristic of quadriceps inhibition.

#### 4.2.6 Statistical Analysis

Statistical analysis was performed using RStudio version 1.2.5033.<sup>179,180</sup>

Descriptive statistics were calculated for participant demographics and components of tendon health for the full sample, male and females, and those with unilateral and bilateral symptoms. Mann-Whitney U tests were used to examine differences between males and females and those with unilateral and bilateral symptoms. The relationships between tendon structure and symptom severity, lower extremity function and quadriceps muscle performance were examined using sequential regression models after adjusting for age, sex, and BMI.<sup>198</sup> Values from the most symptomatic limb were

used for tendon structure, lower extremity function and quadriceps muscle performance. The designation of the most symptomatic limb was based on participant self-reports. Two sequential regression models were performed for each component of tendon health (VISA-P, CMJ height, drop CMJ height, MVIC force, and CAR), with tendon morphology (thickness and CSA) as predictors in the first model and tendon mechanical properties (shear modulus and viscosity) as predictors in the second model. Complete case analysis was used for each model. In the first block, the covariates to adjust for, age, sex and BMI, were entered. Additionally, for measures of lower extremity function (CMJ height and drop CMJ height) and muscle performance (MVIC force and CAR), the respective pain levels recorded during testing were also entered as a covariate. In the second block, the main effects of tendon morphology or mechanical properties were added. The change in  $R^2$  between block 1 and block 2 were tested to see if it significantly improved model fit. Assumptions were examined using visual inspection and Shapiro-Wilk's test for normality. Additionally, data was screened for outliers and extreme cases using visual inspection, Cook's distance, and leverage plots. Alpha level was set at 0.05 for all analysis.

### **4.3 Results**

#### **4.3.1 Participants**

Forty-one injured limbs were included in the analysis. Descriptive statistics are displayed in Table 4.1 for the full sample, males, females, unilateral and bilateral symptoms. Males jumped significantly higher than females in the CMJ and drop CMJ. Otherwise, there were no significant differences between males and females or those with unilateral and bilateral symptoms.

Table 4.1: Descriptive statistics for demographics, symptom severity, lower extremity function and quadriceps muscle performance for the full sample, males and females, and unilateral and bilateral symptoms.

	<b>Total (n = 41) Mean (SD) Median (IQR)</b>	<b>Males (n = 26) Mean (SD) Median (IQR)</b>	<b>Females (n = 15) Mean (SD) Median (IQR)</b>	<b>p-value</b>	<b>Unilateral (n = 28) Mean (SD) Median (IQR)</b>	<b>Bilateral (n = 13) Mean (SD) Median (IQR)</b>	<b>p-value</b>
<b>Age (years)</b>	29.5 (11.3) 27.0 (13.0)	30.4 (12.1) 29.0 (10.3)	28.0 (10.1) 24.0 (8.0)	0.33	29.5 (9.7) 27.5 (11.0)	29.5 (14.6) 25.0 (11.0)	0.50
<b>BMI (kg/m<sup>2</sup>)</b>	25.1 (4.2) 24.7 (5.1)	26.0 (4.5) 25.8 (4.6)	23.5 (3.6) 23.0 (3.7)	0.06	25.3 (3.9) 24.9 (4.7)	24.7 (5.3) 23.0 (6.4)	0.51
<b>VISA-P (points)</b>	57.3 (17.0) 60.0 (24.0)	59.5 (17.8) 60.5 (24.0)	53.6 (15.1) 55.0 (16.0)	0.29	60.1 (16.0) 61.5 (18.8)	51.4 (18.0) 55.0 (29.0)	0.18
<b>CMJ Height (cm)</b>	11.1 (4.9) 12.0 (6.6) n = 35	12.7 (4.6) 13.2 (4.6) n = 24	7.7 (3.7) 7.7 (3.8) n = 11	0.009	11.2 (5.1) 12.1 (7.0) n = 24	10.9 (4.5) 11.4 (6.1) n = 11	0.91
<b>CMJ Pain (NPRS)</b>	2.4 (2.0) 2.0 (4.0) n = 35	2.4 (2.2) 2.0 (4.0) n = 24	2.4 (1.8) 2.5 (2.8) n = 11	0.87	2.2 (2.1) 2.0 (4.0) n = 24	2.8 (1.8) 3.0 (2.3) n = 11	0.32
<b>Drop CMJ Height (cm)</b>	13.1 (5.3) 13.4 (7.5) n = 31	15.3 (4.2) 14.7 (4.5) n = 21	8.4 (4.0) 8.6 (3.9) n = 10	<0.001	12.7 (5.8) 12.8 (7.8) n = 22	14.0 (3.8) 14.3 (2.7) n = 9	0.53
<b>Drop CMJ Pain (NPRS)</b>	2.3 (2.0) 2.0 (4.0) n = 31	1.9 (1.7) 2.0 (3.0) n = 21	2.9 (2.2) 3.0 (3.0) n = 10	0.16	2.2 (1.8) 2.0 (2.0) n = 22	2.3 (2.3) 2.0 (2.0) n = 9	0.81

Table 4.1 continued.

<b>MVIC Force (N)</b>	798.0 (258.2) 839.6 (358.1) n = 22	787.5 (286.3) 799.6 (394.8) n = 16	826.1 (181.1) 869.8 (238.7) n = 6	0.91	746.2 (248.9) 758.2 (386) n = 15	909.1 (260.0) 841.0 (319.8) n = 7	0.30
<b>CAR (%)</b>	78.1 (16.6) 84.6 (24.5) n = 22	74.6 (17.2) 80.3 (29.5) n = 16	87.3 (11.6) 89.4 (8.4) n = 6	0.10	75.4 (18.4) 84.0 (33.7) n = 15	83.9 (10.8) 86.6 (10.9) n = 7	0.49
<b>Burst Pain (NPRS)</b>	1.5 (2.6) 0.0 (2.3) n = 22	1.6 (2.7) 2.0 (3.0) n = 16	1.3 (2.7) 0.0 (0.0) n = 6	0.69	1.2 (2.6) 0.0 (0.0) n = 15	2.3 (2.9) 0.0 (5.0) n = 7	0.39
<b>Tendon Thickness (mm)</b>	6.5 (2.0) 6.3 (3.3) n = 39	7.0 (2.1) 6.9 (2.6) n = 25	5.8 (1.9) 5.3 (3.2) n = 14	0.13	6.6 (2.1) 6.9 (3.3) n = 26	6.4 (2.2) 5.8 (3.3) n = 13	0.97
<b>Tendon CSA (mm<sup>2</sup>)</b>	117.2 (39.9) 106.0 (51.3) n = 38	119.8 (36.6) 111.9 (39.1) n = 24	112.8 (46.1) 94.0 (70.0) n = 14	0.43	118.5 (42.7) 103.2 (58.1) n = 25	114.7 (35.3) 120.0 (34.7) n = 13	0.88
<b>Shear Modulus (kPa)</b>	68.2 (17.9) 68.3 (23.2) n = 35	68.8 (18.1) 70.2 (21.4) n = 24	67.0 (18.0) 59.2 (22.6) n = 11	0.58	69.4 (17.0) 70.2 (17.0) n = 24	65.5 (20.2) 55.5 (22.4) n = 11	0.35
<b>Viscosity (Pa*s)</b>	27.9 (8.6) 28.2 (12.8) n = 35	28.7 (9.7) 28.9 (12.9) n = 24	26.2 (5.8) 24.3 (9.5) n = 11	0.37	28.3 (7.7) 28.9 (12.0) n = 24	27.0 (10.7) 22.7 (12.4) n = 11	0.47

Sample size provided (n) when values were not available for the entire group. BMI = body mass index; CMJ = counter movement jump; NPRS = numeric pain rating scale; MVIC = maximal voluntary isometric contraction; CSA = cross-sectional area.

### 4.3.2 Regression Analysis

Summary tables for regression analyses prior to outlier removal are provided in Appendix A.

#### 4.3.2.1 Symptom Severity

In the initial analysis, two outliers were identified for the relationship to tendon mechanical properties. After removing these cases, all assumptions were met for both sets of predictor variables. There was not a significant relationship between VISA-P scores and tendon morphology ( $p = 0.81$ ,  $R^2$  change = 0.012) or mechanical properties ( $p = 0.19$ ,  $R^2$  change = 0.099) after adjusting for age, sex and BMI.

Table 4.2: Regression analysis for VISA-P with morphology as predictor variables.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.411	0.281	-0.260	0.153	-0.364	0.303	-0.230	0.238
Sex	-8.119	5.702	-0.239	0.164	-7.232	6.108	-0.213	0.245
BMI	0.553	0.717	0.143	0.446	0.547	0.744	0.141	0.468
Thickness					10.487	19.029	0.132	0.585
CSA					-5.911	9.365	-0.142	0.532
$R^2$			0.125				0.137	
F for change in $R^2$			1.621				0.214	

BMI = body mass index; CSA = cross-sectional area.

Table 4.3: Regression analysis for VISA-P with mechanical properties as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	0.249	0.385	0.121	0.523	0.521	0.404	0.253	0.208
Sex	-12.630	6.087	-0.402	<b>0.047</b>	-13.086	5.941	-0.417	<b>0.036</b>
BMI	-0.832	0.852	-0.201	0.337	-0.916	0.883	-0.221	0.309
Shear Modulus					-0.324	0.178	-0.369	0.080
Viscosity					0.413	0.346	0.242	0.243
R <sup>2</sup>		0.131				0.230		
F for change in R <sup>2</sup>		1.456				1.746		

BMI = body mass index.

#### 4.3.2.2 Lower Extremity Function

Two outliers were identified for the relationship between CMJ height and tendon morphology and one outlier was identified for the relationship between drop CMJ height and tendon mechanical properties. After removing these cases, assumptions of normality were met for all analysis. There was a significant positive relationship between CMJ height and tendon thickness ( $p < 0.001$ ,  $\beta = 0.718$ ) and a significant negative relationship between CMJ height and CSA ( $p = 0.001$ ,  $\beta = -0.538$ ), after adjusting for age, sex, BMI, and pain levels. There was a significant positive relationship between CMJ height and viscosity ( $p = 0.006$ ,  $\beta = 0.496$ ) and no significant relationship between CMJ height and shear modulus ( $p = 0.09$ ,  $\beta = -0.278$ ). There was no relationship between drop CMJ height and tendon morphology ( $p = 0.42$ ,  $R^2$  change = 0.037) or mechanical properties ( $p = 0.39$ ,  $R^2$  change = 0.040).

Table 4.4: Regression analysis for counter-movement jump height with morphology as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.147	0.057	-0.369	<b>0.016</b>	-0.093	0.044	-0.234	<b>0.044</b>
Sex	-5.215	1.138	-0.595	<b>&lt;0.001</b>	-3.813	0.881	-0.435	<b>&lt;0.001</b>
BMI	-0.257	0.136	-0.277	0.070	-0.276	0.102	-0.297	<b>0.012</b>
Pain	0.538	0.277	0.246	0.062	0.874	0.231	0.400	<b>0.001</b>
Thickness					14.273	2.847	0.718	<b>&lt;0.001</b>
CSA					-5.360	1.477	-0.538	<b>0.001</b>
R <sup>2</sup>			0.575				0.788	
F for change in R <sup>2</sup>			<b>9.137</b>				<b>12.563</b>	

BMI = body mass index; CSA = cross-sectional area.

Table 4.5: Regression analysis for counter-movement jump height with mechanical properties as predictor variables.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.131	0.082	-0.292	0.123	-0.097	0.074	-0.217	0.204
Sex	-5.824	1.741	-0.571	<b>0.003</b>	-6.150	1.550	-0.603	<b>0.001</b>
BMI	-0.33895	0.204	-0.336	0.109	-0.477	0.186	-0.473	<b>0.017</b>
Pain	0.343	0.355	0.155	0.343	0.301	0.313	0.136	0.347
Shear Modulus					-0.070	0.040	-0.278	0.094
Viscosity					0.253	0.083	0.496	<b>0.006</b>
R <sup>2</sup>			0.382				0.556	
F for change in R <sup>2</sup>			<b>4.018</b>				<b>4.701</b>	

BMI = body mass index.

Table 4.6: Regression analysis for drop counter-movement jump height with morphology as predictor variables.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.015	0.142	-0.017	0.917	-0.006	0.146	-0.006	0.969
Sex	-7.262	1.543	-0.713	<b>&lt;0.001</b>	-6.743	1.605	-0.662	<b>&lt;0.001</b>
BMI	-0.339	0.210	-0.262	0.118	-0.373	0.218	-0.289	0.100
Pain	-0.445	0.454	-0.142	0.336	-0.266	0.496	-0.085	0.597
Thickness					6.156	4.739	0.279	0.207
CSA					-1.762	2.581	-0.150	0.502
R <sup>2</sup>			0.491				0.528	
F for change in R <sup>2</sup>			<b>6.035</b>				0.904	

BMI = body mass index; CSA = cross-sectional area.

Table 4.7: Regression analysis for drop counter-movement jump height with mechanical properties as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	0.060	0.157	0.067	0.705	0.052	0.157	0.058	0.743
Sex	-9.303	1.959	-0.840	<b>&lt;0.001</b>	-9.177	1.965	-0.828	<b>&lt;0.001</b>
BMI	-1.041	0.406	-0.564	<b>0.018</b>	-0.995	0.414	-0.538	<b>0.026</b>
Pain	-0.131	0.502	-0.042	0.796	-0.100	0.504	-0.032	0.844
Shear Modulus					-0.042	0.050	-0.144	0.414
Viscosity					0.137	0.098	0.231	0.180
R <sup>2</sup>			0.553				0.592	
F for change in R <sup>2</sup>			<b>6.791</b>				0.977	

BMI = body mass index.

### 4.3.2.3 Quadriceps Muscle Performance

Three outliers were identified for the relationship between MVIC force and tendon morphology, two for the relationship between MVIC force and mechanical properties, and four for the relationship between CAR and tendon morphology. After removing these cases, assumptions were met for all analysis. There was no relationship between MVIC force and tendon morphology ( $p = 0.27$ ,  $R^2$  change = 0.11) or mechanical properties ( $p = 0.24$ ,  $R^2$  change = 0.12), after adjusting for age, sex, BMI and pain levels. There was a significant negative relationship between CAR and tendon CSA ( $p = 0.04$ ,  $\beta = -0.517$ ) but no significant relationship between CAR and tendon thickness ( $p = 0.38$ ,  $\beta = 0.214$ ). No significant relationship was found between CAR and mechanical properties ( $p = 0.83$ ,  $R^2$  change = 0.01).

Table 4.8: Regression analysis for MVIC force with morphology as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>
Age	16.600	10.370	0.434	0.133	14.060	10.170	0.367	0.194
Sex	13.420	135.580	0.023	0.923	-109.250	176.140	-0.185	0.548
BMI	-39.940	17.460	-0.670	<b>0.040</b>	-34.470	17.940	-0.578	0.081
Pain	-50.730	20.040	-0.534	<b>0.025</b>	-35.820	23.770	-0.377	0.160
Thickness					-251.020	466.580	-0.184	0.601
CSA					-181.220	178.140	-0.273	0.331
$R^2$		0.484				0.593		
F for change in $R^2$		3.049				1.464		

MVIC = maximal voluntary isometric contraction; BMI = body mass index; CSA = cross-sectional area.

Table 4.9: Regression analysis for MVIC force with mechanical properties as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>
Age	14.167	10.992	0.387	0.220	23.799	11.804	0.651	0.069
Sex	-3.860	128.767	-0.006	0.977	29.594	129.922	0.050	0.824
BMI	-38.705	17.726	-0.672	<b>0.048</b>	-40.359	16.973	-0.700	<b>0.037</b>
Pain	-49.507	18.366	-0.586	<b>0.018</b>	-37.109	16.973	-0.439	0.077
Shear Modulus					6.420	3.883	0.473	0.127
Viscosity					-3.032	6.643	-0.118	0.657
R <sup>2</sup>		0.496				0.611		
F for change in R <sup>2</sup>		<b>3.196</b>				1.630		

MVIC = maximal voluntary isometric contraction; BMI = body mass index.

Table 4.10: Regression analysis for CAR with morphology as predictor variables after removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.559	0.372	-0.250	0.159	-0.208	0.358	-0.093	0.573
Sex	11.806	5.879	0.369	0.068	18.289	6.079	0.571	<b>0.013</b>
BMI	-2.547	1.218	-0.385	0.059	-0.908	1.546	-0.137	0.570
Pain	-4.416	1.054	-0.705	<b>0.001</b>	-5.157	1.065	-0.823	<b>0.001</b>
Thickness					20.687	22.429	0.214	0.378
CSA					-23.570	9.853	-0.517	<b>0.038</b>
R <sup>2</sup>		0.683				0.798		
F for change in R <sup>2</sup>		<b>6.455</b>				2.863		

CAR = central activation ratio; BMI = body mass index; CSA = cross-sectional area.

Table 4.11: Regression analysis for CAR with mechanical properties as predictor variables.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.381	0.449	-0.191	0.409	-0.331	0.482	-0.166	0.505
Sex	19.249	7.681	0.499	<b>0.024</b>	20.731	8.516	0.537	<b>0.030</b>
BMI	1.081	0.768	0.318	0.180	1.004	0.837	0.295	0.252
Pain	-3.974	1.090	-0.676	<b>0.002</b>	-4.035	1.186	-0.687	<b>0.005</b>
Shear Modulus					-0.024	0.203	-0.027	0.908
Viscosity					0.233	0.420	0.135	0.589
R <sup>2</sup>			0.572				0.584	
F for change in R <sup>2</sup>			<b>5.015</b>				0.187	

CAR = central activation ratio; BMI = body mass index.

#### 4.4 Discussion

In this study, measures of tendon structure were found to relate to lower extremity function and muscle performance, but not symptom severity, after adjusting for age, sex, BMI and activity provoked pain-levels. There was a positive relationship between viscosity and CMJ height, indicating that individuals with lower viscosity had worse jumping performance. There was also a significant relationship between maximum tendon thickness and CSA and CMJ height, although the direction of these relationships was opposite. Individuals with thinner tendons and larger CSA had worse jump performance. Furthermore, there was a negative relationship between CSA and quadriceps CAR, suggesting that individuals with larger CSA have decreased quadriceps activation. All other relationships did not achieve significance. However, it should be noted that there was some evidence suggesting a relationship between tendon mechanical properties and morphology and MVIC force, although we were not adequately powered to reach significance. Based on the observed change in

$R^2$  for mechanical properties, the effect size was medium and an additional 19 participants (at 80% power, alpha 0.05) would be needed to detect a significant relationship. Similarly, for morphology, the effect size was medium and an additional 22 participants would be needed for significant relationship.

#### **4.4.1 Adjusting for Covariates**

There are a number of variables that may influence tendon structure, lower extremity function, and quadriceps muscle performance. Therefore, we chose to adjust for age, sex, and BMI, as well as activity provoked pain for select outcome measures, in our analysis.

Age is associated with a decline in muscle strength and recruitment, which may influence results of jump tests and quadriceps muscle performance.<sup>199–201</sup> The influence of age on mechanical properties is less clear. In animal models, the mechanical properties of tendon have been shown to increase,<sup>202–204</sup> decrease,<sup>205–208</sup> or remain unchanged as a result of ageing.<sup>209–211</sup> In vitro and in vivo studies of human tendon have found an increase,<sup>212,213</sup> a reduction,<sup>160,214–219</sup> or no change in mechanical properties in response to age.<sup>160,214,220–222</sup> In a recent study using cSWE, our research group found that age was negatively related to static shear modulus in females and positively related to viscosity, regardless of sex, for uninjured Achilles tendons.<sup>223</sup> The influence of age on tendon morphology is also unclear, as animal models and human studies have found that tendon CSA either increases<sup>212,217,218,224–226</sup> or does not change due to aging.<sup>204,221,222</sup> Although the effect of age on tendon health requires further study, we felt that there was sufficient evidence to necessitate adjusting for its effect in our models.

The influence of sex on the constituents of patellar tendon health have been more thoroughly documented. Males have greater knee extension strength,<sup>227–230</sup> patellar tendon thickness<sup>230–233</sup> and CSA,<sup>234</sup> and jump height compared to females,<sup>51,235,236</sup> even when accounting for training history<sup>227,234</sup> and muscle size.<sup>228</sup> There is also conflicting evidence that males have greater patellar tendon stiffness than females.<sup>230,234,237,238</sup> Therefore, it was important to control for the influence of sex in our analysis.

BMI has been shown to positively relate to measures of tendon morphology.<sup>110,212,239</sup> Additionally, relationships have been observed between BMI and patellar tendon stiffness, although the direction of these relationship varies.<sup>110,212</sup> A positive relationship has been observed between BMI and patellar tendon stiffness in an athletic population,<sup>212</sup> while a negative relationship has been observed in a sedentary population.<sup>110</sup> The discrepancy likely a reflection of the activity levels and body composition of the two samples, as greater BMI may reflect a more muscular build in an athletic population and greater adiposity in a sedentary population. Furthermore, quadriceps muscle morphology (thickness and CSA) have been shown to positively relate to knee extension strength.<sup>240–243</sup> In this study, measures of quadriceps muscle morphology were not performed. However, those with large muscle size would likely have a higher BMI. Therefore, we used BMI as a surrogate measure to account for these effects.

Finally, induced knee pain has been shown to reduce quadriceps strength and activation,<sup>244</sup> while reduction of pain via analgesia has been show to increase quadriceps activity following open ACL reconstruction.<sup>245</sup> There is also conflicting evidence that pain severity is related to the magnitude of quadriceps activation deficits

in individuals undergoing total knee arthroplasty.<sup>246,247</sup> Therefore, knee pain potentially influences knee extension strength and activation. Furthermore, since the quadriceps muscles account for 41% of the work performed during the take-off phase of the CMJ, it is reasonable to assume that knee pain may also influence the measures of lower extremity function.<sup>49</sup>

#### **4.4.2 Symptom Severity**

This study found no relationship between tendon structure and symptom severity. Few studies have examined the relationship between tendon structure and measures of symptom severity in patellar tendinopathy, but those that have, found contradictory results.<sup>35,40,90,165</sup> In these studies, measures of symptom severity have included VISA-P scores and subscales, pain-pressure threshold at the patellar tendon, and pain during the single-leg decline squat test. Furthermore, it is important to note that in these studies, the authors did not control for potential confounding factors, such as age, sex or BMI. Studies utilizing elastography to assess measures of tendon stiffness have found that stiffness may be positively<sup>35,165</sup> or negatively<sup>90</sup> related to symptom severity. Another study using mechanical dynamometry combined with ultrasound imaging to assess tendon mechanical properties found a negative relationship between tendon strain and pain levels but tendon stiffness did not relate to measures of symptom severity.<sup>40</sup> Additionally, no relationships have been observed between limb symmetry indexes of patellar tendon thickness or CSA with symptom severity, while raw values of thickness may be unrelated, positively related, or negatively related to symptom severity, depending on the time since shockwave treatment.<sup>35,165</sup> To summarize, prior studies are inconclusive regarding the relationship

between tendon structure and symptom severity but our findings support those studies that found no relationship.

#### **4.4.3 Lower Extremity Function**

Our findings indicate that viscosity and maximum patellar tendon thickness are positively related to CMJ height, CSA is negatively related to CMJ height and tendon structure does not relate to drop CMJ height. To our knowledge, only one study has examined the relationship between patellar tendon structure and jump performance. Their results suggested that a larger, less stiff tendon is associated with better jumping ability.<sup>101</sup> However, our results are not directly comparable since the prior study was performed in healthy individuals and tendon structure is altered by patellar tendinopathy.<sup>30,31,40,32-39</sup>

Viscosity is a rate dependent measure of stretch.<sup>248</sup> In other words, the elongation of viscous materials is dependent on the rate of loading. Therefore, a tendon will deform less when loaded quickly versus when it is loaded slowly.<sup>248</sup> Additionally, a tendon with higher viscosity will deform less than a tendon with lower viscosity at the same loading rate.<sup>248</sup> The CMJ is a ballistic movement, requiring rapid force transmission from muscle to bone. Thus, it is not surprising that there is a positive relationship between viscosity and CMJ height, as a more viscous tendon will deform less and be more efficient at force transfer.<sup>248</sup> On the other hand, at the micro-structural scale, tendinopathy is accompanied by an increase in proteoglycans, hypervascularization, and increased water content.<sup>20,249,250</sup> These changes may reduce the viscosity of tendon, leading to less efficient force transfer and decreased lower extremity function.<sup>251</sup>

Interestingly, we observed that tendon thickness and cross-sectional area had opposite relationships with CMJ height. Tendon thickness was positively related while CSA was negatively related. A potential explanation for this discrepancy is that CSA is more responsive to patellar tendinopathy induced changes in tendon morphology. Additionally, this would suggest that patellar tendon thickness is more of a reflection of loading history, which may explain why a positive relationship was observed between thickness and jump height. One can appreciate why CSA measures may be more sensitive to pathological changes when looking at Figure 4.5. These are representative CSA images of an a) uninjured and b) injured tendon in a collegiate athlete. The yellow outline is the CSA measure and the red dashed line is the approximate location at which thickness measures are taken on long-axis images. This participant had focal thickening in the medial portion of the tendon, which did not align with the location of thickness measures. Giacchino et al. found that patellar tendon CSA was better able to discriminate between asymptomatic volleyball players with “subclinical tendinopathy” than patellar tendon thickness.<sup>252</sup> In their study, “subclinical tendinopathy” was defined as light structural abnormalities with neovascularization or moderate/severe structural abnormalities with or without neovascularization. In our study, the cross-sectional area was 22% larger on average in the most symptomatic limb compared to the least symptomatic limb while tendon thickness was 17% larger. However, it is unclear to what degree these structural changes were present prior to injury, since the tendon is mechanoresponsive and hypertrophies in response to loading.<sup>253,254</sup> Furthermore, the degree of morphological change may be influenced by sports participation, especially when that sport preferentially loads one limb.<sup>212,254</sup> Therefore, further investigation is needed to

determine whether the magnitude of morphological changes due to patellar tendinopathy are similar for thickness and CSA.

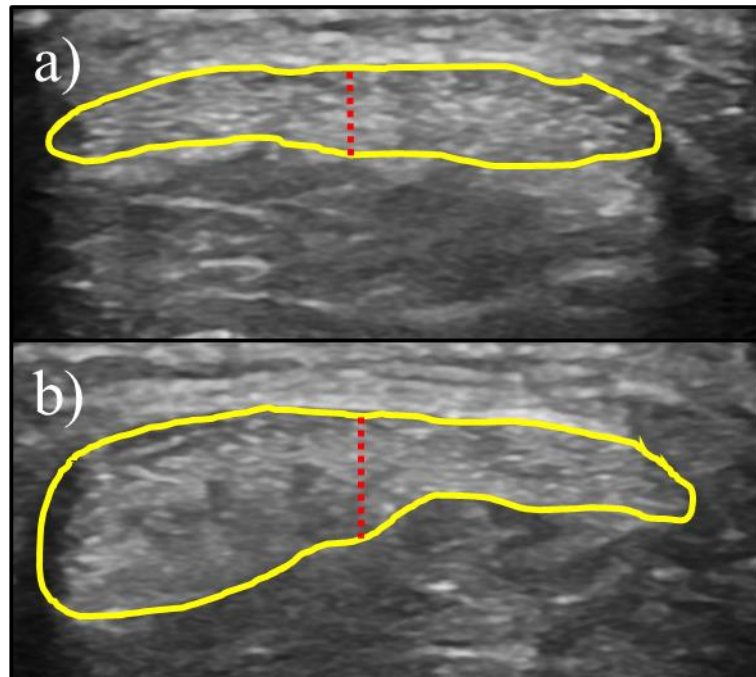


Figure 4.5: Short axis images of an (a) uninjured and (b) injured patellar tendon in a collegiate athlete. Medial focal thickening is present in the injured tendon. The yellow line represents the CSA measurement and the red dashed line represents the approximate location where thickness measures are taken on long axis images.

It is unclear why similar relationships were not observed for the drop CMJ. Anecdotally, we have observed that participants are more apprehension when performing the drop CMJ, since it involves dropping off of a box, which may influence their performance and presence of such relationships.

#### 4.4.4 Quadriceps Muscle Performance

We found a negative relationship between patellar tendon CSA and quadriceps CAR, indicating that greater CSA is associated with decreased quadriceps activation. This is the first study to examine relationships between patellar tendon structure and quadriceps activation but not the first study to observe altered quadriceps activity in the presence of patellar tendinopathy. Rio et al. found that isometric quadriceps contractions resulted in an immediate reduction in pain, decreased inhibitory neural drive to the quadriceps, and increased knee extension MVIC.<sup>42</sup> In a follow-up study, the same research group found that individuals with patellar tendinopathy have elevated corticospinal excitability to the quadriceps, which may impair their ability to match quadriceps activation to task requirements.<sup>41</sup> Additionally, this altered excitability was not present in patients with anterior knee, or patellofemoral pain. Therefore, pain is unlikely to be the sole explanation for these changes in quadriceps activity. Furthermore, similar associations between altered tendon structure and muscle activity have been found in other forms of tendinopathy. Chang and Kulig investigated the impact of altered Achilles tendon structure without pain, or Achilles tendinosis, on triceps surae activity.<sup>29</sup> They found that these individuals had decreased activity in the triceps surae of the involved limb compared to the uninvolved limb during a hopping task.

It should also be noted that there was some evidence suggesting a relationship between tendon mechanical properties and morphology with MVIC force, although we were not adequately powered to reach significance. Based on the observed change in  $R^2$  for mechanical properties, the effect size was medium and an additional 19 participants would be needed to detect a significant relationship at 80% power and an alpha level of 0.05. Similarly, for morphology, the effect size was medium and an

additional 22 participants would be needed for significance. In healthy individuals, increased tendon size and stiffness are positively related to quadriceps strength.<sup>110,255</sup> However, it is unclear if the relationships would be similar in an injured population so further investigation with a larger sample size is needed.

#### **4.4.5 Limitations**

We acknowledge that there are several limitations to this study. First, this study had a relatively small sample size. Therefore, we may not have been adequately powered to detect all relationships between tendon structure and the outcome variables of interest. However, in a post-hoc analysis we assessed the effect sizes of non-significant models to determine if a relationship may exist in a larger population. With the exception of knee extension MVIC relationships, effect sizes were small or negligible. Second, there was a relatively large proportion of missing data, especially for measures of quadriceps muscle performance. Knee extension strength and quadriceps activation testing were added to the study after initiation so early participants did not complete these tests. For other measures, the missing data was due to a combination of equipment failure or intentionally dropping values due to exclusion criteria. Since some data was intentionally removed, it was not appropriate to utilize multiple imputation, which assumes that the data is missing at random.<sup>256</sup> Third, we did not control for physical activity level in our models, which may also influence measures of tendon structure. Physical activity level was recorded using the Physical Activity Scale, which is a 6-point ordinal scale with scores ranging from 1 to 6 (1 = Sedentary, 6 = Highly active).<sup>257</sup> However, there is a ceiling effect for this measure in highly active populations, such as those with patellar tendinopathy. 83% of our participants had a score of 5 or above, so we did not feel that this measure

accurately captured differences in physical activity level between participants. Finally, cSWE has several known limitations stemming from its use of the Voight model to calculate shear modulus and viscosity, which assumes a linear isotropic material under no stress.<sup>91,193</sup> Although the patellar tendon is a non-linear, anisotropic material, we believe that this will have minimal influence on the obtained values, as described in our previous work.<sup>223</sup>

#### **4.5 Conclusions**

In this exploratory study, we investigated the relationships between altered tendon structure with symptom severity, lower extremity function and quadriceps muscle performance in individuals with patellar tendinopathy. We found that tendon structure influences lower extremity function and quadriceps muscle performance, even after adjusting for age, sex, BMI and activity-provoked pain. Alterations in tendon structure persist after symptom resolution, therefore, addressing these changes may play a role in optimizing outcomes of patellar tendinopathy treatment. Furthermore, this suggests that treatment studies for patellar tendinopathy should monitor tendon structure, in addition to symptoms. However, prospective studies with larger sample sizes are needed to determine if changes in tendon structure relate to improvements in other constituents of tendon health.

## Chapter 5

### **PAIN-GUIDED ACTIVITY MODIFICATION DURING TREATMENT FOR PATELLAR TENDINOPATHY: A FEASIBILITY AND PILOT RANDOMIZED CLINICAL TRIAL**

#### **5.1 Introduction**

Patellar tendinopathy is an overuse injury to the patellar tendon, usually resulting from excessive overload to the tendon with inadequate time for recovery.<sup>112</sup> Therefore, activity modification is considered to be a key component of patellar tendinopathy treatment.<sup>2</sup> Activity modification is usually paired with exercise therapy, consisting of tendon loading exercises, which is the treatment that currently has the highest level of evidence supporting its efficacy.<sup>13,14</sup> Clinicians typically modify the intensity, duration and/or type of activities performed outside of treatment to ensure that the tendon can sufficiently recover between bouts of tendon loading exercises.<sup>112</sup>

Although activity modification is recognized as a key component of patellar tendinopathy treatment, implementation of activity modification in treatment studies varies widely. Recommendations for altering recreational physical activity have ranged from complete cessation of sports participation<sup>21,22,24</sup> to continued activity at the pre-injury level.<sup>17,18,82</sup> Other studies have used a more individualized approach where pain-levels are used to guide activity modification.<sup>19,20</sup> Each of these approaches have yielded positive results, however, the impact of activity modification on treatment outcomes have not been directly investigated or compared. Therefore, it

is unclear whether activity modification recommendations were beneficial or detrimental to treatment outcomes.

The optimal amount of activity modification likely lies somewhere between activity cessation and full participation since either end of the spectrum may have negative consequences. Absence from sport due to injury has been associated with increased anxiety, depression and reduced self-esteem.<sup>114</sup> Additionally, activity cessation may reduce the tendon's tolerance to sport-specific loads and decrease physical fitness. As a result, these athletes may be at increased risk for re-injury or the development of new injuries. On the other hand, full participation may reduce or nullify the benefits of exercise therapy.<sup>82</sup> Therefore, it is of interest to identify a middle-ground between activity cessation and full participation, which limits negative psychological consequences of injury, maintains physical readiness for sport, and maximizes recovery.

Pain-guided activity modification using the Pain-Monitoring Model may be a suitable middle-ground for activity modification. Originally described by Thomeé et al. for use in patellofemoral pain, the Pain-Monitoring Model provides guidelines for acceptable pain-levels during activity.<sup>258</sup> Briefly, pain levels should not exceed a 5/10 on the numeric pain rating scale (NPRS) during or immediately after activity. Additionally, pain ratings should return to pre-activity levels by the following morning. In a prior randomized clinical trial (RCT), the Pain-Monitoring Model was adapted for use in Achilles tendinopathy.<sup>115</sup> In this study, continued activity using the Pain-Monitoring Model had no detrimental effects on treatment outcomes when compared to a group with pain-free activity modification. This approach to activity modification has been previously utilized for patellar tendinopathy, however, the

impact on treatment outcomes has not been investigated or compared with other recommendations.<sup>19,20</sup>

Ultimately, our research group aims to compare the impact of continued activity using the Pain-Monitoring Model on treatment outcomes in patellar tendinopathy with other approaches to activity modification. However, prior to initiating a large RCT, it is critical to establish the feasibility of the study design.<sup>116</sup> This is especially important in patellar tendinopathy, since this injury is most common in team sports and using individualized activity recommendations may pose unforeseen challenges. Additionally, it is important to assess whether the proposed outcome measures are able to capture changes in response to the intervention. This ensures that the participants are not subjected to undue burden and resources are allocated to worthwhile measures. Therefore, the purpose of this study is two-fold:

1. To assess the feasibility of a randomized clinical trial utilizing pain-guided activity modification while undergoing standardized treatment for patellar tendinopathy.
2. To evaluate the ability of proposed outcome measures to capture changes in tendon health over the course of treatment.

## **5.2 Methods**

### **5.2.1 Study Design**

This study was a pilot and feasibility randomized clinical trial with parallel assignment. The study was approved by the University of Delaware Institutional Review Board, prospectively registered (ClinicalTrials.gov ID: NCT03694730), and conducted according to CONSORT guidelines.<sup>259,260</sup> To be included, participants had

to have a clinical diagnosis of patellar tendinopathy and be between the ages of 16 and 40 years old. The diagnostic criteria for patellar tendinopathy was 1) pain and stiffness localized to the patellar tendon and 2) load-dependent symptoms, which increased as demands placed on the patellar tendon increased.<sup>2,170</sup> Potential participants were excluded if they had an injury, other than patellar tendinopathy, that limited their ability to participate in treatment and/or testing. Additionally, individuals were excluded if they had knee surgery or an injection, tenotomy, or shockwave to the patellar tendon within the last 6 months. All participants received written and oral information about the study prior to participation and provided informed consent.

Participants were randomly assigned into one of two treatment groups: 1) a *Pain-Guided Activity (PGA)* group and 2) a *Pain-Free Activity (PFA)* group. All participants completed patellar tendon loading exercises three times a week for 12 weeks using a standardized treatment program.<sup>19,20</sup> During the first six weeks of treatment, participants were asked to limit their physical activity outside of treatment, according to their group assignment. Participants in the PGA group were allowed to continue their usual recreational activities, using the pain-monitoring model to guide activity intensity (Figure 5.1).<sup>115</sup> The PFA group were not allowed to perform running, jumping, or activities that provoke their patellar tendon pain outside of treatment. However, they were allowed to perform activities that were not pain-provoking, such as freestyle swimming or the elliptical. Additionally, participants completed evaluations at baseline, 6- and 12-weeks to assess symptom severity, psychological factors, tendon morphology and mechanical properties, lower extremity function, and quadriceps muscle performance.



### **5.2.3 Treatment Protocol**

All participants completed a modified version of the Heavy-Slow Resistance protocol three times a week for 12-weeks.<sup>19,20</sup> The original protocol consists of three exercises, the squat, leg press, and hack squat. In the modified version, the hack squat was replaced with the knee extension due to equipment availability. Participants complete four sets of each exercise per session using a 6-second count per repetition (3 second eccentric, 3 second concentric phase). An auditory metronome was used to pace each repetition. Over the course of the protocol, the load is progressively increased and repetitions are decreased (Figure 5.2). Resistance levels for each phase of the treatment protocol are dosed based on the participants 5-repetition max for each exercise, which were performed at the initial treatment and approximately every two weeks after. At 6- and 12-weeks, participants were asked to rate their level of satisfaction on a 10-point Likert scale (0 = Not satisfied, 10 = Very Satisfied).

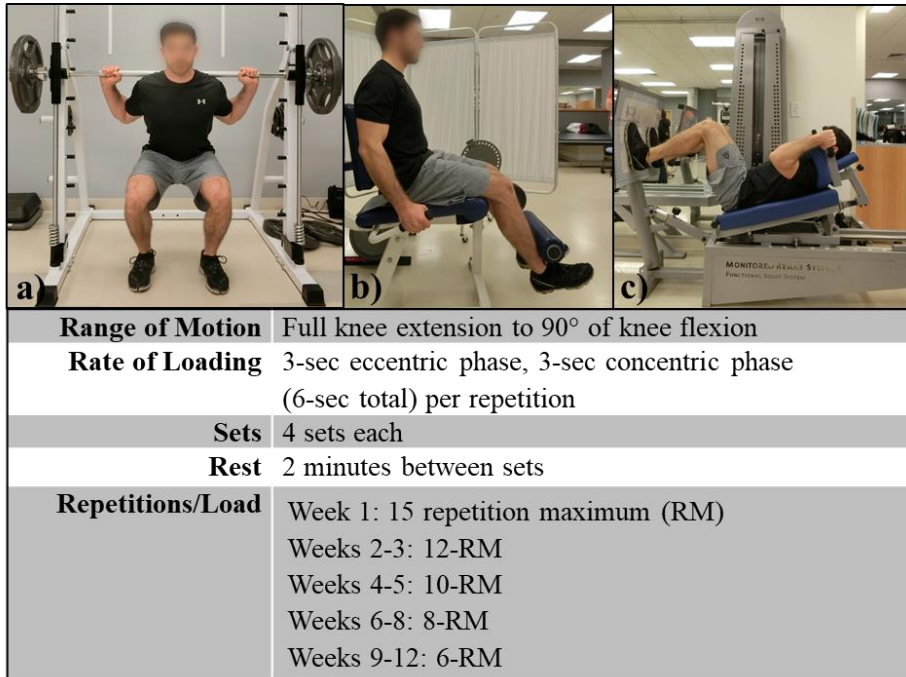


Figure 5.2: Heavy-Slow Resistance training parameters for the A) squat, B) knee extension and C) leg press.

#### 5.2.4 Compliance, Retention and Safety

Compliance with exercises and activity modifications were tracked using paper training diaries (Appendix C). For each day, participants were asked to record the treatment exercises completed, whether they performed running and/or jumping activity, any other physical activity performed, and their pain levels upon waking. Furthermore, if participants performed physical activity other than treatment exercises, they were asked to rate their pain levels prior to, during, and after the activity. The training diaries were collected weekly and reviewed by the research team. For each week, the number of times treatment exercises were completed, days the training diary was completed, days of running or jumping activity, and days in compliance with activity restrictions (weeks 1-6) was recorded. Participants were considered compliant

with treatment if they performed at least two of the three prescribed exercise sessions per week. Additionally, the number of missed follow-up evaluations, drop-outs, and adverse events were recorded.

## **5.2.5 Treatment Outcomes**

### **5.2.5.1 Symptom Severity**

Symptom severity was assessed using the Victorian Institute of Sports Assessment – Patellar Tendon (VISA-P) questionnaire. The VISA-P is an 8-item questionnaire designed to assess patellar tendinopathy symptom severity and the impact on physical function.<sup>6</sup> Scores range from 0 to 100 with lower scores indicating greater disability. This instrument has a minimally clinically important difference (MCID) of 13 points.<sup>261</sup>

### **5.2.5.2 Psychological Factors**

Participants fear of movement and re-injury, or kinesiophobia, were captured using the Tampa Scale of Kinesiophobia (TSK-17).<sup>262,263</sup> Higher levels of kinesiophobia have been associated with worse recovery of lower extremity function in Achilles tendinopathy.<sup>264</sup> Additionally, in pilot studies, we found that the majority of patients with patellar tendinopathy have clinically meaningful levels of kinesiophobia.<sup>265</sup> Scores range from 17 to 68 points, with higher scores indicating a greater fear of movement and re-injury.

The presence and severity of negative emotional states was measured using the Depression, Anxiety, and Stress Scale (DASS-21).<sup>266</sup> The DASS-21 has previously been used to evaluate the mental health of athletes at a variety of competition levels.<sup>267,268</sup> The DASS-21 consists of 21 questions that can be divided into three

subscales, 1) Depression, 2) Anxiety, and 3) Stress. Scores range from 0 to 63 points, with higher scores indicating a greater degree of negative emotional states.

### **5.2.5.3 Tendon Morphology**

B-mode ultrasound imaging was performed at the patellar tendon using a LOGIC *e* Ultrasound (GE Healthcare, Chicago, IL) system with a wide-band linear array probe (5.0 – 13.0 MHz) to assess tendon morphology. Participants were positioned in supine with the knee flexed to 30° and supported by a bolster.<sup>176</sup> Three extended field of view long-axis images were completed on each limb from the tibial tuberosity to the inferior pole of the patellar to obtain maximal tendon thickness. Additionally, three short-axis images were taken at 1 cm distal to the inferior pole of the patella on each limb to obtain cross-sectional area (CSA). A custom MATLAB code was used to identify the maximal tendon thickness and Osirix MD imaging software (Pixmeo, Geneva, Switzerland) was used to measure CSA. The average of three images was used for analysis.

### **5.2.5.4 Tendon Mechanical Properties**

Continuous shear wave elastography (cSWE) was used to evaluate patellar tendon mechanical properties with a Sonix MDP Q+ (Ultrasonix, Vancouver, BC, Canada) ultrasound scanner with a L14-5/38 probe.<sup>91,169</sup> For this technique, participants were seated on an adjustable plinth with their legs stabilized at 90° of hip and knee flexion. The inferior pole of the patella and the tibial tuberosity were identified and a mark was placed 1 cm distal to the inferior pole of the patella, along the imaginary line connecting the two bony landmarks. The ultrasound probe was centered over this mark, in line with the long axis of the tendon. A Minishaker Type

4810 (Brüel and Kjaer, Norcross, GA, USA) was placed on the quadriceps tendon and used to produce shear waves at 11 different frequencies (322, 339, 358, 379, 402, 429, 460, 495, 536, 585, and 643 Hz). As each frequency propagated through the patellar tendon, the ultrasound probe captured raw radiofrequency data at 6438 frames/sec. A custom MATLAB code was used for post-processing to provide estimates of static shear modulus and viscosity, as described by Cortes et al and Corrigan et al.<sup>91,169</sup> Three trials were performed per limb and the average of three trials was used for analysis.

#### **5.2.5.5 Lower Extremity Function**

The single-leg counter-movement jump (CMJ) and single-leg drop CMJ were used to evaluate lower extremity function.<sup>196</sup> These tests have high reliability and have previously been used to assess function in Achilles tendinopathy.<sup>115,196</sup> For the CMJ, participants began by standing on a single leg on flat ground with their hands behind their back. They were instructed to jump as high as they can, landing on the same leg with which they took off from the ground.<sup>196</sup> The drop CMJ was performed similarly except that participants assumed the starting position on a 20 cm high box. They were instructed to “drop” off of the box and then jump as high as they can once they contacted the ground.<sup>196</sup> For both tests, an infrared light mat (MuscleLab®, Ergotest Innovations, Stathelle, Norway) was used to record flight time, which was then used to estimate jump height. The average of three trials was used for analysis.

#### **5.2.5.6 Quadriceps Muscle Performance**

A knee extension maximal voluntary isometric contraction (MVIC) with the burst-superimposition method was used to evaluate knee extension strength and

quadriceps muscle activation.<sup>197</sup> This technique has demonstrated reliability and has been utilized in a variety of chronic knee injuries.<sup>197,269–275</sup> Participants were seated on a KinCom dynamometer (Model 50 H, Isokinetic International, Chattanooga, TN, USA) at 90° of hip flexion and 60° of knee flexion for the tested limb. Self-adhesive electrodes were placed over the distal vastus medialis and proximal vastus lateralis muscle bellies. After familiarization with procedures and a standardized warm-up, participants were instructed to perform a 5-second MVIC. During the MVIC, a supramaximal, 10-pulse (600 μs, 130 V, 100 pulses per second) train of electrical stimulation was applied to the muscle using an electrical stimulator (Grass Technologies, Champaign, IL). Verbal encouragement was provided throughout each trial. If the participant was unable to activate quadriceps fully or they did not reach and maintain their peak MVIC prior to delivery of the burst, testing was repeated up to 4 times, with 3 minutes rest between trials. The MVIC force and force attributable to the electrical stimulation was recorded. The best trial, based on force production and visual inspection of the force production graph, was selected to calculate quadriceps central activation ratios (CAR = [MVIC force/burst augmented force] x 100%). The CAR is a measure of quadriceps inhibition, where lower values indicate a greater degree of quadriceps inhibition.

### **5.2.6 Alterations to Study Protocol After Initiation**

Due to the COVID-19 pandemic, in-person human subjects research was halted at the University of Delaware on March 17<sup>th</sup>, 2020. At that time, there were seven active participants in the study. One had completed treatment and was scheduled for their 12-week follow-up, the remaining participants had completed their 6-week evaluations and were in the final phase of the treatment protocol. For those

participants still in treatment, a modified version of the treatment protocol was created utilizing resistance bands so participants could continue treatment without access to fitness facilities (Appendix D). Bands of varying resistance (Rogue Monster Bands, Rogue Fitness, Columbus, OH) were mailed to the participants to ensure that they could replicate the resistance of isotonic exercises as closely as possible. Additionally, remaining follow-up evaluations were completed remotely, with the participants completing questionnaires online. Measures of tendon morphology and mechanical properties, lower extremity function and quadriceps muscle performance were not collected for these participants.

### **5.2.7 Statistical Analysis**

Statistical analysis was performed using R version 3.6.3 and IBM SPSS version 25 (Chicago, IL) statistics software.<sup>179,180</sup> The target sample size was determined a priori based on a minimally clinically important improvement of 13 points in the VISA-P from baseline to 12-weeks using values obtained from a prior study.<sup>20,261</sup> It was determined that 10 participants would be required per group with 80% power and alpha set at 0.05. To account for drop-out, the target recruitment was set at 15 participants per group (30 total).

Descriptive statistics were calculated for demographic information at baseline and outcome measures at each timepoint for both groups. Demographic characteristics between groups were compared using Student's T-tests for normally distributed variables or Mann-Whitney U tests when the assumption of normality was not met. To assess compliance, the proportion of prescribed treatment sessions completed, weeks in compliance with treatment, days in compliance with activity restrictions, and the number of days of running or jumping per week were calculated for each group.

A 2x3 Generalized Linear Mixed Model (GLMM) was used to test the change over time for both groups for the primary outcomes: symptom severity, psychological factors, tendon morphology and mechanical properties, lower extremity function and quadriceps muscle performance using the intention to treat principle.<sup>276-279</sup> For morphology, mechanical properties, lower extremity function and quadriceps muscle performance, the most symptomatic limb was used for the analysis. If participants had bilateral symptoms, they were asked to identify their most symptomatic limb in their baseline questionnaires. Time point (Baseline, 6- and 12-weeks) and group (PGA or PFA) were entered as fixed effects. A compound symmetric covariance matrix was used to model the correlation among residuals, using the covariance structure is equivalent to including random intercepts. GLMM models are able to garner accurate estimates in the presence of missing data without excluding entire cases, assumed that is at least missing at random.<sup>279</sup> Allowing for anyone with an observation at a time point to be included at that time.

To test the assumption of normality and to look for outliers, model residuals were tested using Shapiro-Wilks tests, and screened for outliers. If time was significant, all pair-wise comparisons were tested post-hoc. Mean differences between timepoints were compared to the smallest detectable change (SDC) and minimally clinically important difference (MCID) to assess the magnitude of effect for all outcomes (Appendix E). Alpha was set at 0.05 for all tests.

## **5.3 Results**

### **5.3.1 Recruitment**

Recruitment ran from January 15<sup>th</sup>, 2019 to February 1<sup>st</sup> 2020. A total of 108 individuals completed the initial screening online or by phone (Figure 5.3). Thirty-one potential participants completed the in-person screening (Figure 5.3). Of these individuals, 16 were deemed not to be eligible and one declined to participate (Figure 5.3). Fifteen participants were randomized (PGA: 9; PFA: 6). In total, 43.5% (47/108) of interested individuals were eligible for participation and 32.0% (15/47) of those that were eligible were willing to be randomized (Figure 5.3).

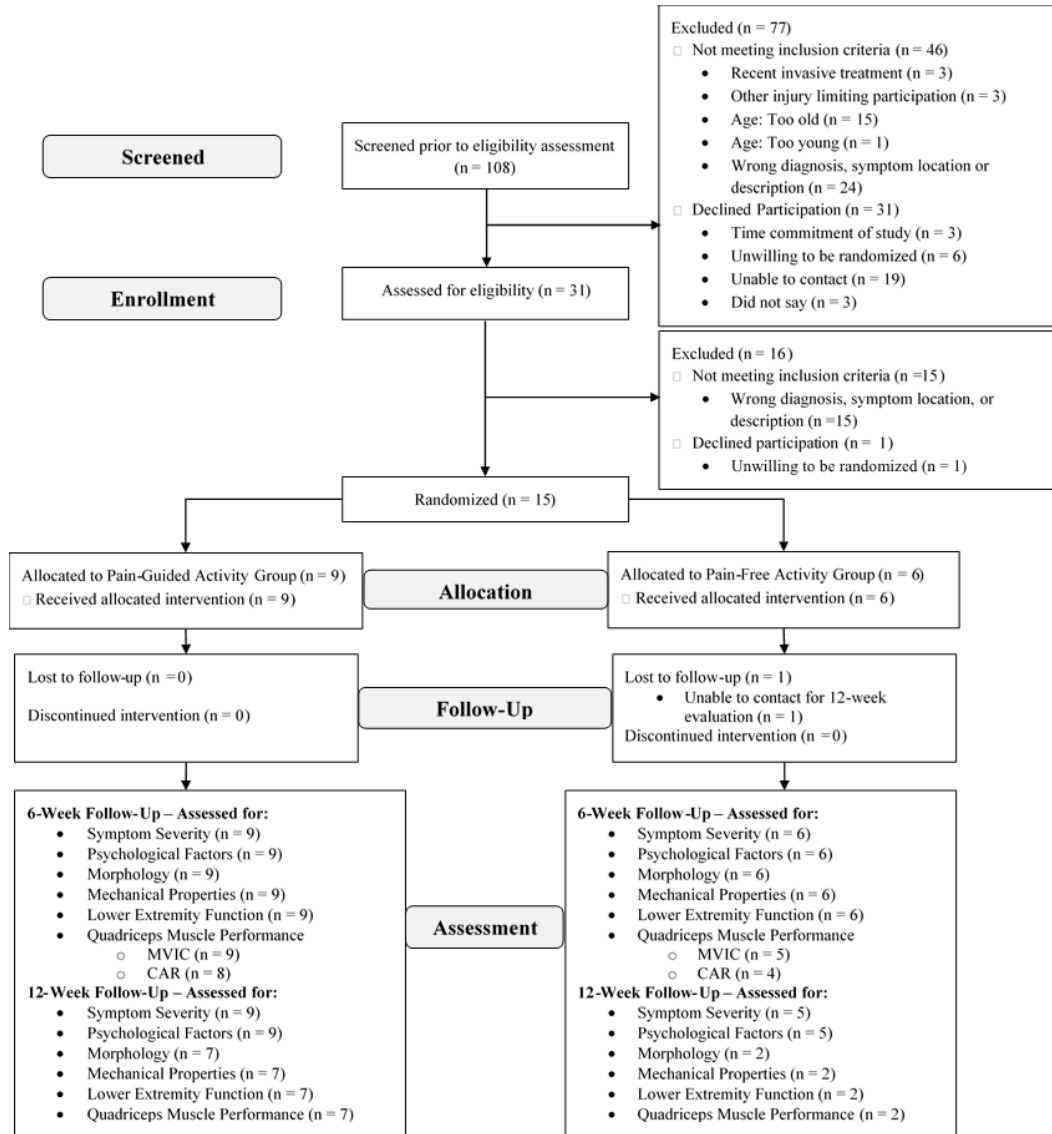


Figure 5.3: CONSORT flowchart for recruitment and randomization.<sup>259</sup>

### 5.3.2 Participants

Participant demographics and training history are summarized in table 5.1. There were no significant differences between groups in any of the displayed characteristics ( $p > 0.05$ ). There were two participants in the PGA group and three in the PFA group with bilateral symptoms.

Table 5.1: Baseline demographics and training history for pooled sample and group assignments.

	<b>Pooled Sample Mean (SD) Median (IQR) (n = 15, 5 F)</b>	<b>Pain-Guided Mean (SD) Median (IQR) (n = 9, 3 F)</b>	<b>Pain-Free Mean (SD) Median (IQR) (n = 6, 2 F)</b>
<b>Age (years)</b>	26.6 (3.9) 27.0 (7.0)	26.9 (3.5) 28.0 (4.0)	26.3 (4.8) 25.0 (7.8)
<b>Height (cm)</b>	175.9 (9.8) 172.7 (13.0)	176.9 (11.0) 174.6 (4.0)	174.4 (8.4) 172.4 (7.3)
<b>Weight (kg)</b>	79.4 (16.9) 80.1 (19.6)	79.9 (12.7) 82.2 (5.5)	78.6 (23.3) 68.2 (20.4)
<b>BMI (kg/m<sup>2</sup>)</b>	25.5 (4.3) 24.7 (4.5)	25.4 (3.0) 25.9 (4.1)	25.6 (6.1) 23.5 (2.4)
<b>Symptom Duration (months)</b>	32.2 (42.1) 15.8 (36.4)	21.2 (27.4) 7.5 (28.4)	48.8 (56.7) 28.4 (69.3)
<b>VISA-P (points)</b>	58.9 (17.9) 60.0 (19.0)	65.7 (15.8) 69.0 (20.0)	48.8 (17.1) 51.5 (18.3)
<b>Weekly Hours Training/Playing Primary Sport (hrs/wk)</b>	6.1 (5.2) 4.0 (5.0)	5.7 (5.9) 3.0 (5.0)	6.8 (4.5) 6.0 (4.3)
<b>Weekly Hours Training/Playing Other Sports (hrs/wk)</b>	1.8 (1.9) 2.0 (1.0)	2.0 (2.4) 2.0 (1.0)	1.5 (1.0) 1.5 (1.0)
<b>Weekly Hours of Jump Training (hrs/wk)</b>	1.0 (1.0) 1.0 (1.0)	1.3 (1.2) 1.0 (0.5)	0.5 (0.6) 0.5 (1.0)
<b>Weekly Hours of Strength Training (hrs/wk)</b>	4.6 (4.1) 4.0 (3.5)	5.6 (4.7) 4.0 (4.0)	3.0 (2.4) 3.0 (3.5)

BMI = body mass index; There were no significant differences between the pain-guided and pain-free activity groups.

### 5.3.1 Compliance, Retention, and Safety

Participants compliance with treatment, training diaries and activity restrictions are summarized in table 5.2. There was one participant lost to follow-up from the PFA group who did not complete their 12-week evaluation. Additionally, this participant had completed the treatment portion of the study but had not provided their training

diaries. There were two adverse events during the course of the study, both in the PFA group. In both instances, the participants experienced a new onset of lateral knee pain while performing activities unrelated to study participation, at their home or their gym. However, in both cases, these new symptoms were aggravated by tendon loading exercises and required modification to knee angles and/or prescribed loads to limit discomfort. For both participants, symptoms resolved without additional treatment.

Table 5.2: Participants compliance with treatment, training diaries, and activity modification.

	<b>Pain-Guided Mean (SD) Median (IQR)</b>	<b>Pain-Free Mean (SD) Median (IQR)</b>	<b>Pain-Free – Complete Cases* Mean (SD) Median (IQR)</b>
<b>Proportion of prescribed treatment sessions completed (%)</b>	86.1 (13.0) 83.3 (22.2)	67.1 (30.7) 77.8 (20.1)	78.9 (11.7) 80.6 (11.1)
<b>Proportion of weeks compliant with treatment (%)</b>	92.3 (9.4) 91.7 (8.3)	76.4 (37.8) 91.7 (6.3)	91.7 (5.9) 91.7 (0.0)
<b>Proportion of days training diary was completed (%)</b>	98.4 (2.7) 100.0 (2.4)	81.3 (40.0) 98.8 (7.7)	97.6 (4.1) 100.0 (2.4)
<b>Proportion of days compliant with activity restrictions (%)</b>	97.3 (3.9) 100.0 (5.4)	80.2 (39.8) 98.8 (13.1)	96.2 (7.3) 100.0 (2.4)
<b>Days of running or jumping per week (days/wk)<sup>#</sup></b>	1.9 (1.4) 1.5 (2.0)	0.0 (0.2) 0.0 (0.0)	0.0 (0.2) 0.0 (0.0)

\*Participant that was lost to follow-up was dropped for the complete cases analysis.

<sup>#</sup>First six weeks used.

### 5.3.2 Satisfaction with Treatment

Satisfaction with treatment at 6-week and 12-week follow-ups are summarized in table 5.3.

Table 5.3: Participants satisfaction with treatment at 6- and 12-weeks.

	6-Week Follow-Up		12-Week Follow-Up	
	Mean (SD)		Mean (SD)	
	Median (IQR)		Median (IQR)	
	Pain-Monitoring	Pain-Free	Pain-Monitoring	Pain-Free
<b>Satisfaction with Treatment (points)</b>	9.0 (1.1)	7.3 (2.3)	9.3 (1.1)	8.4 (2.1)
	9.0 (2.0)	7.0 (4.3)	10.0 (1.0)	9.0 (2.0)

### 5.3.3 Treatment Outcomes

The estimated marginal means, standard error and pair-wise comparisons of timepoints for the pooled sample are displayed in table 5.4. The F-statistic and significance level for group and time effects, as well as results prior to outlier removal are displayed in Appendix F.

Table 5.4: Estimated marginal means, standard error and pair-wise comparisons of timepoints for the pooled sample.

Category	Outcome	Baseline		6-Weeks		12-Weeks		p-values		
		M	SE	M	SE	M	SE	Baseline to 6-Weeks	Baseline to 12-Weeks	6-Weeks to 12-Weeks
<b>Symptoms</b>	VISA-P (points)	59.6	3.8	68.8	3.8	75.6	4.0	<b>0.043</b>	<b>0.001</b>	0.136
<b>Psychological Factors</b>	TSK (points)	36.4	1.1	35.8	1.1	34.2	1.1	0.448	<b>0.015</b>	0.075
	DASS-21 (points)	3.2	1.0	3.4	1.1	5.6	1.1	0.847	0.040	0.061
<b>Morphology</b>	Thickness (mm)	6.9	0.5	6.8	0.5	6.6	0.6	0.427	0.329	0.678
	CSA (mm <sup>2</sup> )	111.9	11.0	118.0	10.6	118.0	12.0	0.355	0.443	1.000
<b>Mechanical</b>	Shear Modulus (kPa)	70.6	6.3	77.1	6.2	79.8	9.2	0.427	0.391	0.796
	Viscosity (Pa*sec)	31.6	2.4	29.7	2.3	33.0	3.1	0.396	0.628	0.268
<b>Lower Extremity Function</b>	CMJ Height (cm)	12.1	1.2	13.3	1.2	13.7	1.3	<b>0.033</b>	<b>0.045</b>	0.620
	Drop CMJ Height (cm)	13.4	1.2	13.9	1.3	13.4	1.4	0.423	0.953	0.588
<b>Quadriceps Muscle Performance</b>	MVIC (N)	860.9	56.7	995.9	60.0	1053.4	85.6	0.138	0.082	0.601
	CAR (%)	80.6	3.3	84.1	3.8	90.7	4.9	0.440	0.076	0.250

CSA = cross-sectional area; CMJ = counter-movement jump; MVIC = maximal voluntary isometric contraction; CAR = central activation ratio

### 5.3.3.1 Symptom Severity

There were significant effects of time and group for VISA-P,  $F = 6.59$ ,  $p = 0.005$  and  $F = 6.06$ ,  $p = 0.029$ , respectively. There was a significant difference between baseline ( $M = 59.6$ ,  $SE = 3.8$ ) and both 6 weeks ( $M = 68.8$ ,  $SE = 3.8$ ) and 12-week ( $M = 75.6$ ,  $SE = 4.0$ ) follow-ups,  $p = 0.043$  and  $p = 0.001$ , respectively (Figure 5.4). There was no difference between 6-week and 12-week follow-ups,  $p = 0.136$ . The PGA group ( $M = 75.1$ ,  $SE = 3.6$ ) was significantly higher than PFA ( $M = 60.8$ ,  $SE = 4.5$ ). All differences between timepoints exceeded the SDC and differences between baseline and 12-weeks exceeded the MCID.<sup>261</sup>

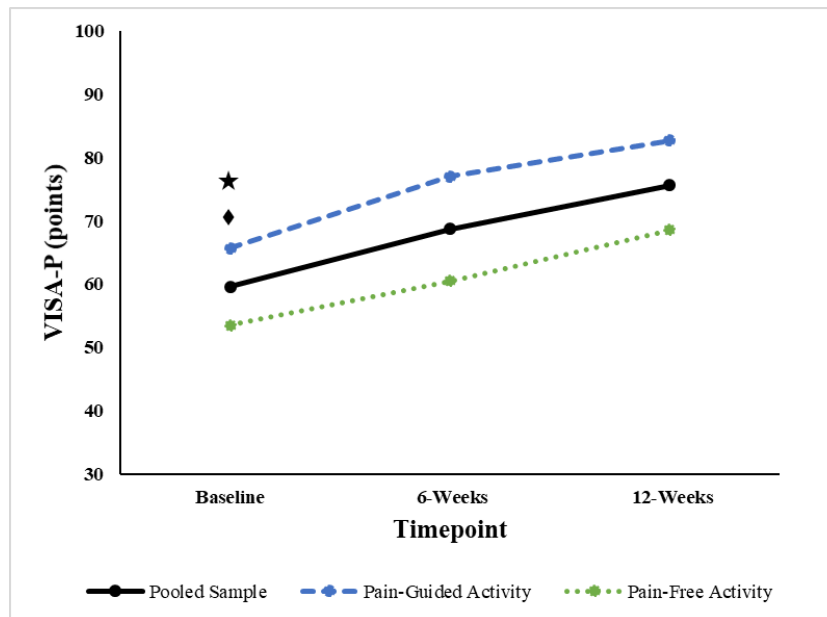


Figure 5.4: Estimated marginal means for symptom severity for the pooled samples and groups. ★ = significantly different from 6-weeks; ◆ = significantly different from 12-weeks. Note: Statistical significance is for the pooled sample only and Y-axis is truncated.

### 5.3.3.2 Psychological Factors

There was a significant effect of time, but not group, for the TSK,  $F = 3.53$ ,  $p = 0.045$  and  $F = 1.43$ ,  $p = 0.25$ , respectively. There was a significant difference between baseline ( $M = 36.4$ ,  $SE = 1.1$ ) and 12-weeks ( $M = 34.2$ ,  $SE = 1.1$ ),  $p = 0.015$  (Figure 5.5). There was no difference between baseline and 6-weeks ( $p = 0.45$ ) or 6-weeks and 12-weeks ( $p = 0.08$ ). All differences between timepoints exceeded the SDC.

In the initial analysis, two outliers were identified for the DASS-21. After removal of these outliers, assumptions of normality were met. There was a significant effect of group, but not time, for the DASS-21,  $F = 6.68$ ,  $p = 0.005$  and  $F = 2.80$ ,  $p = 0.08$ , respectively (Figure 5.6). The PGA group ( $M = 2.7$ ,  $SE = 1.1$ ) was significantly lower than the PFA group ( $M = 5.5$ ,  $SE = 1.4$ ). Differences between baseline and 12-weeks and 6-weeks and 12-weeks exceeded the SDC.

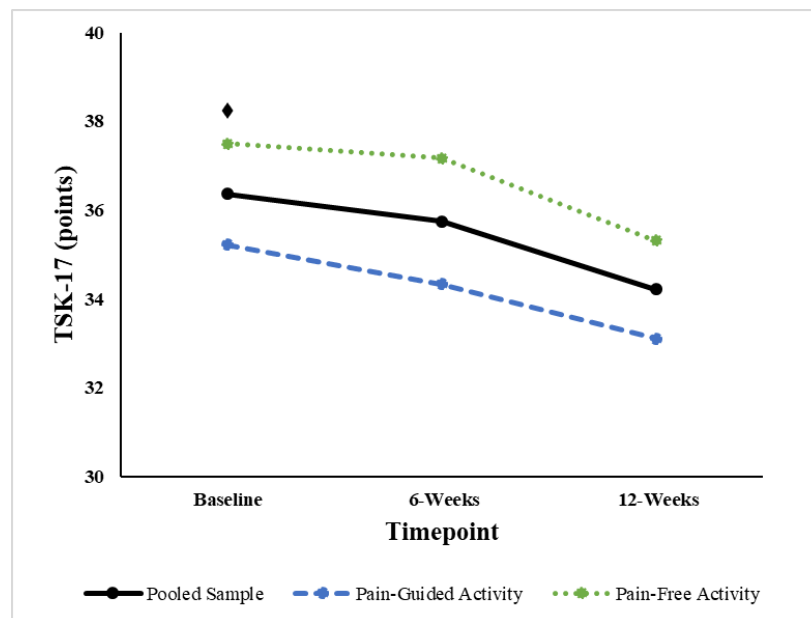


Figure 5.5: Estimated marginal means for TSK-17 for the pooled sample and groups.  $\blacklozenge$  = significantly different from 12-weeks. Note: Statistical significance is for the pooled sample only and the Y-axis is truncated.

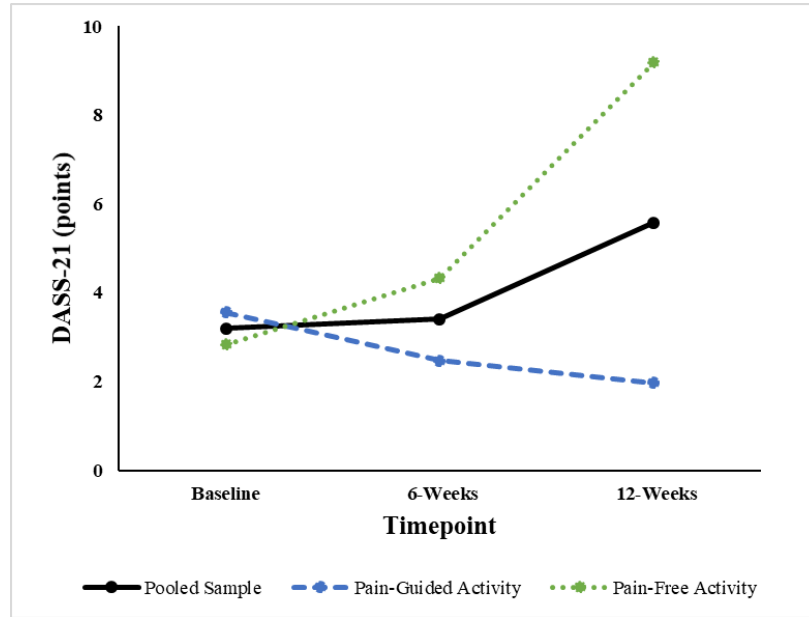


Figure 5.6: Estimated marginal means for DASS-21 for the pooled sample and groups. Note: Y-axis is truncated.

### 5.3.3.3 Tendon Morphology

In the initial analysis, two outliers were identified for CSA. After removal of these outliers, all assumptions of normality were met. The effects of time and group were not significant for thickness (*Time*:  $F = 0.62$ ,  $p = 0.55$ ; *Group*:  $F = 0.07$ ,  $p = 0.79$ ) or CSA (*Time*:  $F = 0.58$ ,  $p = 0.57$ ; *Group*:  $F = 0.40$ ,  $p = 0.54$ ) (Figures 5.7 and 5.8). For thickness, differences from baseline to 6-weeks and 12-weeks exceeded the SDC. Differences between timepoints did not exceed the SDC for CSA.

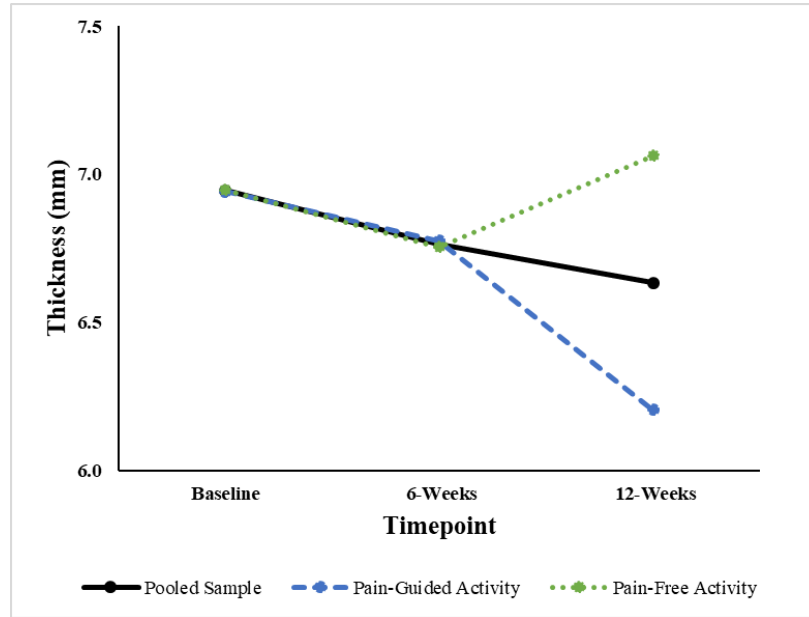


Figure 5.7: Estimated marginal means for tendon thickness for the pooled sample and groups. Note: Y-axis is truncated.

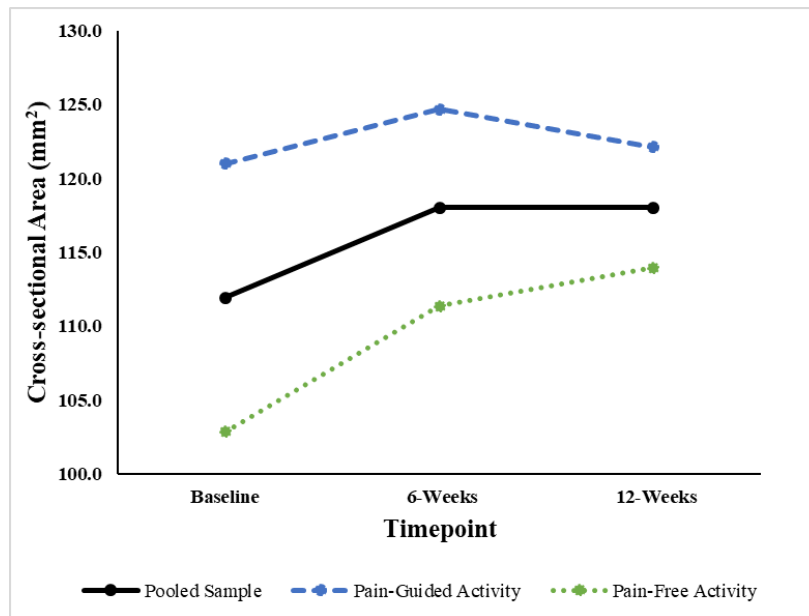


Figure 5.8: Estimated marginal means for tendon cross-sectional area for the pooled sample and groups. Note: Y-axis truncated.

### 5.3.3.4 Tendon Mechanical Properties

The effects of time and group were not significant for static shear modulus (*Time: F = 0.51, p = 0.61; Group: F = 0.49, p = 0.50*) or viscosity (*Time: F = 0.77, p = 0.48; Group: F = 0.11, p = 0.75*) (Figures 5.9 and 5.10). Differences between timepoints did not exceed the SDC for shear modulus. All differences between timepoints exceeded the SDC for viscosity.

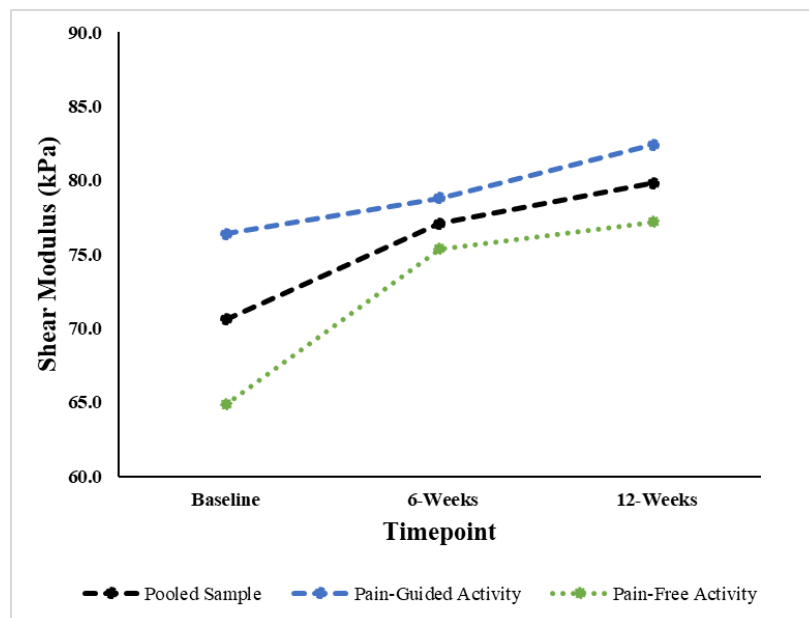


Figure 5.9: Estimated marginal means for shear modulus for the pooled sample and groups. Note: Y-axis truncated.

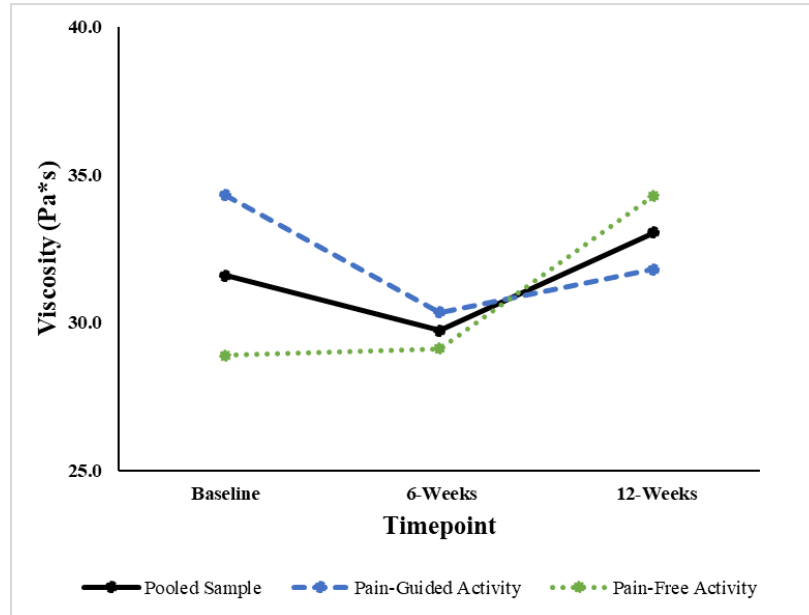


Figure 5.10: Estimated marginal means for viscosity for the pooled sample and groups. Note: Y-axis truncated.

### 5.3.3.5 Lower Extremity Function

There was a significant effect of time, but not group, for CMJ height,  $F = 3.61$ ,  $p = 0.046$  and  $F = 0.01$ ,  $p = 0.92$ , respectively. There was a significant difference between baseline ( $M = 12.1$ ,  $SE = 1.2$ ) and both 6-week ( $M = 13.3$ ,  $SE = 1.2$ ) and 12-week ( $M = 13.7$ ,  $SE = 1.3$ ) follow-ups,  $p = 0.033$  and  $p = 0.045$ , respectively (Figure 5.11). There was no difference between 6-week and 12-week follow-ups,  $p = 0.62$ . Differences from baseline to 6-week and 12-week follow-ups exceeded the SDC.

The effects of time and group were not significant for drop CMJ height,  $F = 0.37$ ,  $p = 0.70$  and  $F = 0.13$ ,  $p = 0.73$ , respectively (Figure 5.12). Differences between timepoints did not exceed the SDC.

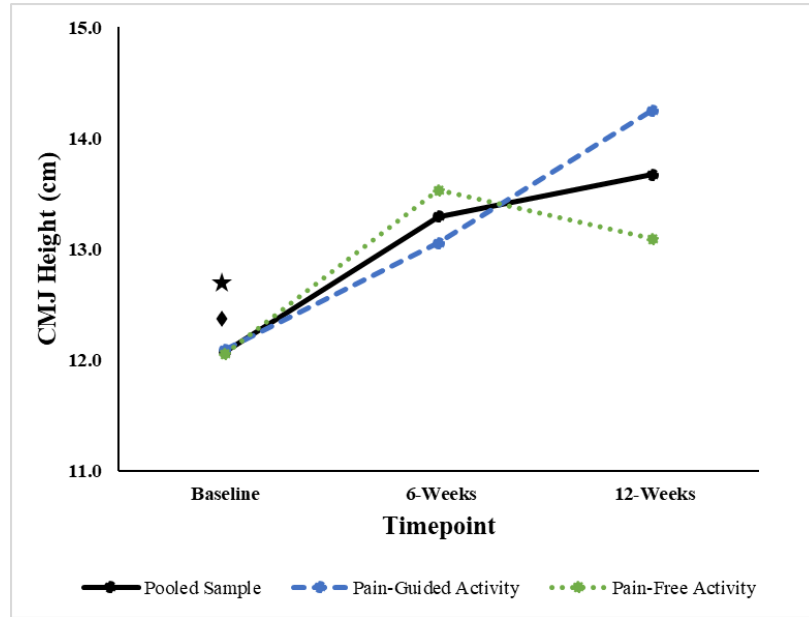


Figure 5.11: Estimated marginal means for CMJ height for the pooled sample and groups. ★ = significantly different from 6-weeks; ◆ = significantly different from 12-weeks. Note: Statistical significance is for the pooled sample only and the Y-axis is truncated.

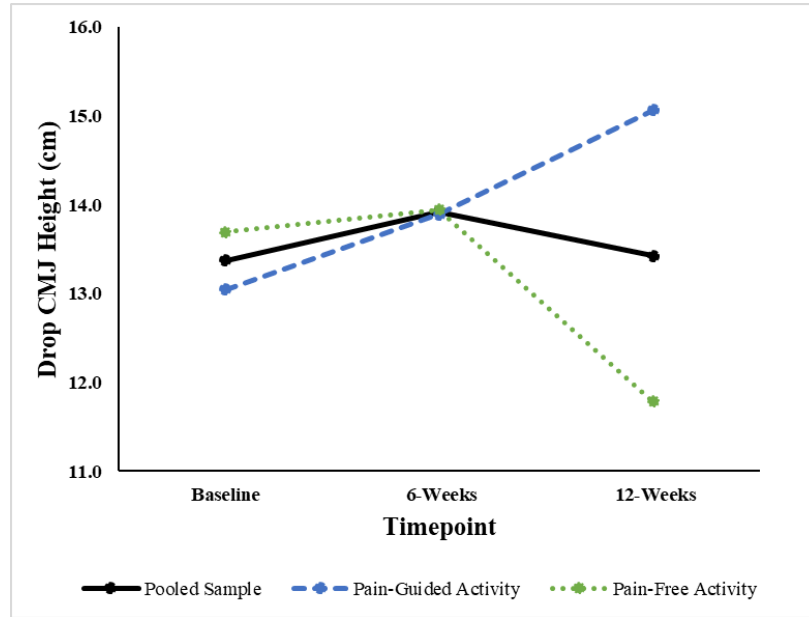


Figure 5.12: Estimated marginal means for drop CMJ height for the pooled sample and groups. Note: Y-axis is truncated.

### 5.3.3.6 Quadriceps Muscle Performance

The effects of time and group were not significant for knee extension MVIC (*Time: F = 2.07, p = 0.15; Group: F = 3.74, p = 0.08*) or CAR (*Time: F = 1.79, p = 0.20; Group: F = 3.33, p = 0.10*) (Figures 5.13 and 5.14). All differences between timepoints exceeded the SDC for both measures.

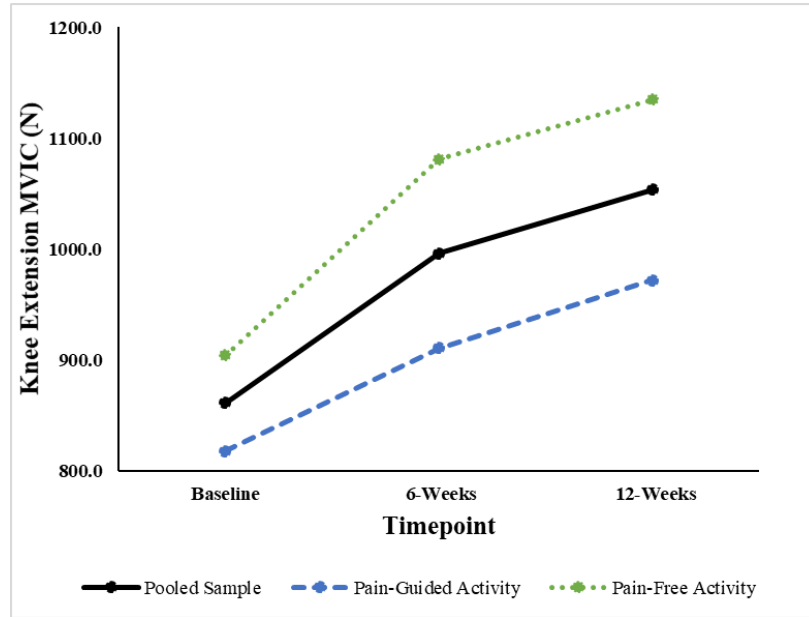


Figure 5.13: Estimated marginal means for knee extension MVIC for the pooled sample and groups. Note: Y-axis is truncated.

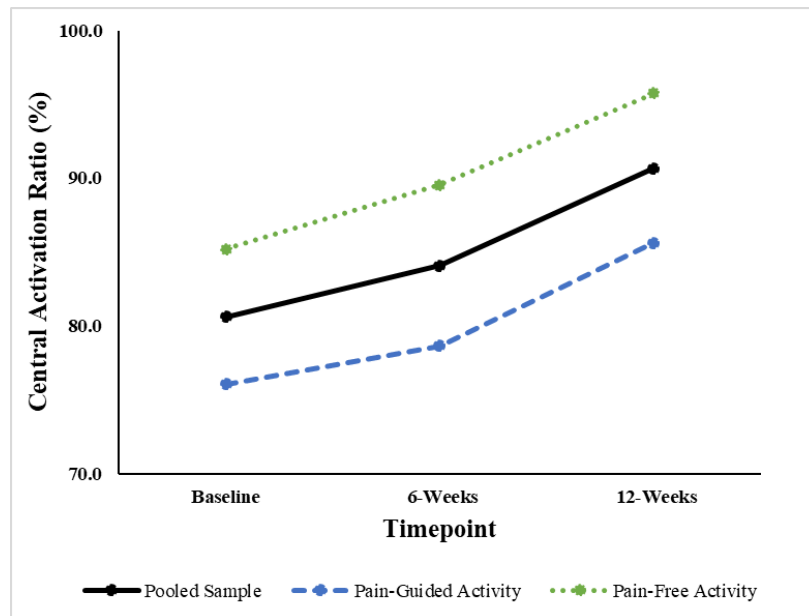


Figure 5.14: Estimated marginal means for central activation ratio for the pooled sample and groups. Note: Y-axis is truncated.

## **5.4 Discussion**

This pilot and feasibility randomized clinical trial had two aims. The first was to assess the feasibility of using the Pain-Monitoring Model to guide activity modification during treatment for patellar tendinopathy. The second was to evaluate whether the planned outcome measures would be able to detect differences in different areas of tendon health over the course of treatment.

### **5.4.1 Recruitment and Randomization**

Fifteen of the 30 planned participants were consented and randomized to an intervention group in the ~13-month recruitment window. Although this fell short of our recruitment goal, the rate of recruitment was not consistent throughout the recruitment window. In the first nine months of recruitment, six participants joined the study compared to nine participants in the final four months (Appendix B). This increase in recruitment towards the end of the study can be attributed to identification of new community collaborations, primarily adult recreational sports leagues with a large social media and community presence. In the full randomized clinical trial, we would use a non-inferiority design where the primary hypothesis is that the pain-monitoring group would not be substantially worse than the pain-free group at 12-weeks.<sup>280</sup> In other words, we would need to be adequately powered to detect a minimally clinically important difference of 13 points in the VISA-P score at 12-weeks. With alpha set at 0.025 and 80% power, we would need 32 participants per group and would recruit 80 participants to account for drop-out. At our recruitment rate in the final four months, it would take approximately 3 years to recruit all participants, which we deemed to be a realistic timeline.

The current randomization scheme resulted in uneven group assignment since we did not reach our target recruitment. Therefore, when conducting the full RCT, the randomization should include blocking to ensure relatively equal assignment throughout the study. Additionally, there was inadequate allocation concealment, as the randomization scheme was stored as a spreadsheet, which was accessible by the member of the research team that was recruiting and consenting participants. This has the potential for introducing bias, as this member of the research team may be aware of future assignments during recruitment. A full clinical trial should utilize computer based allocation concealment, as described by Vickers, so that members of the research team are not aware of assignment until after the participant has been consented.<sup>281</sup> Despite these limitations, the randomization scheme performed well, as the baseline characteristics were similar between groups.

#### **5.4.2 Compliance and Retention**

A priori compliance targets were not established. However, compliance outcomes can be compared to prior clinical trials using similar methods. The Heavy-Slow Resistance protocol was originally described and utilized in an RCT by Kongsgaard et al.<sup>20</sup> In their study the mean compliance rate for treatment was  $91 \pm 5\%$ . Compliance rates were slightly lower for the PGA group ( $86.1 \pm 13.0\%$ ) and substantially lower in the PFA group ( $67.1 \pm 30.7\%$ ) and variability in compliance was larger for both groups than in the previous study. Additionally, Kongsgaard et al. had no drop-outs or losses to follow-up at their 12-week timepoint, while we had one participant lost to follow-up. In the prior study, they found that 70% of participants were satisfied with their clinical outcome at 12-weeks. Although the question wording was not identical, our participants mean satisfaction with treatment was 9.3 out of 10

points and 8.4 out of 10 points for the PGA and PFA groups, respectively. It's important to note that compliance may have been influenced by the COVID-19 pandemic. For example, the participant lost to follow-up had been scheduled for their 12-week evaluation but it had to be cancelled due to a hold on human subjects research. After this cancellation, we were unable to contact the individual to complete the online portion of the evaluation. Additionally, this individual did not provide their training diaries so only treatments supervised by a member of the research team could be counted when assessing treatment compliance. However, they had reported compliance with their home exercises at prior treatments, so their compliance was likely higher than recorded.

Training diaries are widely used in orthopedic research to assess compliance but the completion rate of these training diaries is rarely reported.<sup>16,18,82,88,115,282</sup> Therefore, it is challenging to compare our compliance rates with training diaries and activity modification to prior studies. A recent pilot and feasibility study for plantar fasciopathy by Riel et al followed compliance with a home exercise program for eight weeks using training diaries.<sup>283</sup> Their reported completion rate was 75%. Our completion rate was substantially higher for the PGA group and slightly higher for the PFA group. To our knowledge, no prior studies have reported compliance with activity restrictions using the pain-monitoring model or with other forms of activity modification in patellar tendinopathy. Participants completing training diaries tend to overestimate their compliance with interventions but have higher compliance than if training diaries are not required.<sup>284</sup> Thus, the primary purpose of our training diaries was to encourage compliance, with awareness that the values may not reflect participant's true compliance. Additionally, this is more in line with clinical practice,

where clinicians provide recommendations to patients but cannot assess how closely the patients adhere to those recommendations. Other forms of activity tracking were explored to monitor compliance; however, activity trackers are not able to capture pain levels. Therefore, they would not be able to identify if participants followed activity restrictions.

### **5.4.3 Safety**

Assessing safety is another key component of pilot and feasibility trials. In our study, we had two adverse events. In both instances, participants experienced a new onset of lateral knee pain, which were aggravated by the treatment exercises. Given that the symptoms initially appeared while completing activities unrelated to study participation, it is unlikely that these events can be attributable to the study interventions.

### **5.4.4 Treatment Outcomes**

The purpose of pilot and feasibility studies is not to assess the efficacy or effectiveness of an intervention, in this case, activity modification.<sup>116</sup> Thus, we intentionally did not test the group by time interaction to determine if the magnitude of change in outcome measures was different between groups. However, it is of interest to determine if the proposed outcome measures have adequate sensitivity to capture the effect of the interventions.<sup>116</sup> Therefore, we analyzed the effect of time in the pooled sample and compared mean differences between timepoints to the SDC and MCID of the respective measures.

Significant differences between timepoints were observed for the VISA-P score, TSK scores, and CMJ height, indicating that the Heavy-Slow Resistance

protocol had an appreciable effect on symptom severity and lower extremity function, Therefore, this treatment protocol appears appropriate for use in a larger RCT. Furthermore, differences between at least two timepoints exceeded the SDC for all outcome measures, except for CSA, static shear modulus and drop CMJ height. Thus, we have at least one outcome measure for each domain of tendon health that can potentially detect the effect of our interventions.

A potential benefit of utilizing a pain-guided approach to activity is that it may reduce the negative psychological consequences of injury.<sup>114</sup> However, scores on the DASS-21 were low, indicating low levels of depression, anxiety, and/or stress. Furthermore, when comparing individual sub-scores to established cut-offs, none of the participants had clinically meaningful levels of depression, anxiety and/or stress at baseline.<sup>285,286</sup> This may be due in part to the nature of the participants recruited. Only one participant was currently playing a sport at the collegiate level or above. Individuals that participate in sport at higher levels of competition typically derive more of their social identity and self-worth from their role as an athlete.<sup>287</sup> Thus, they may suffer a greater degree of negative psychological consequences in response to injury. This suggests that in a full RCT greater effort should be made in recruiting high level athletes and stratification for competition level may be necessary during randomization.

Although depression, anxiety, and stress were not prevalent in this sample, kinesiophobia levels were high. At baseline, 7 out of 15 participants met or exceed a previously established threshold (37 points) for “high kinesiophobia” and all participants scored a 30 or above.<sup>288</sup> Additionally, TSK scores decreased from baseline to 6- and 12-weeks. These changes were significant for baseline to 12-weeks and all

differences between timepoints exceeded the SDC. Therefore, it may be of interest to track this metric in full RCT to determine how activity modification recommendations impact fear of movement and re-injury.

#### **5.4.5 Limitations**

This study has several limitations, including uneven randomization and poor allocation concealment, which were discussed previously. Additionally, examiners were not blinded to group assignment, which may introduce bias when collecting baseline and follow-up measures. It is not desirable to blind the treating physical therapist to group assignment, as we believe that communication between the clinician and the participant about their weekly activity will promote adherence to activity modification. Since this was a pilot and feasibility study, one member of the research team performed all treatments and evaluations so it was not possible to keep the examiner blinded. Another limitation was the use of paper training diaries. The primary purpose of these diaries was to promote adherence, not assess compliance. However, there is evidence that suggests that study participants are more diligent and honest when completing electronic diaries.<sup>289</sup> Thus, we may have greater confidence in the accuracy of their self-reported compliance. Additionally, use of electronic diaries would allow us to send reminders and limit lost data. Finally, seven participants were impacted by COVID-19, which either limited their ability to complete treatment and/or follow-up evaluations. As a result, those participants that were still participating in treatment may not have received the same magnitude of loading as those that completed treatment prior to the pandemic. Also, the estimated marginal means for 12-week follow-ups was based on a reduced sample size, which may over- or under-estimate the magnitude of change in the missing outcome measures.

## **5.5 Conclusions**

The use of a pain-guided activity modification during treatment for patellar tendinopathy appears feasible, based on the recruitment, compliance and retention observed in this study. Additionally, the proposed outcome measures appear appropriate, as we observed changes that exceeded the SDC for each domain of tendon health. Although significant improvements were detected in symptom severity and lower extremity function in the pooled sample, a larger, more stringent RCT is needed to assess the impact of pain-guided activity modification on treatment outcomes during exercises therapy for patellar tendinopathy.

## **Chapter 6**

### **CONCLUSION**

Patellar tendinopathy is rampant among athletes that participate in jumping sports, with 11.8-14.4% of recreational<sup>3</sup> and 32-45% of elite volleyball and basketball players experiencing symptoms.<sup>4</sup> These athletes suffer from pain,<sup>1,2</sup> reduced sports performance<sup>7,9,10</sup> and lost playing time<sup>7,10-12</sup> but the consequences also extend beyond the court. Individuals with patellar tendinopathy report impaired function, which can interfere with activities of daily living and work demands.<sup>5-8</sup> Treatment outcomes are currently sub-optimal, as patients only achieve 52-79% of full recovery following 12-weeks of treatment<sup>19,20,22,23,26,27</sup> and 27-51% will experience reinjury.<sup>11,12</sup> A potential explanation for these sub-optimal outcomes is that treatment for patellar tendinopathy tends to focus solely on pain resolution while ignoring the fact that the injury is accompanied by alterations in tendon structure,<sup>30,31,40,32-39</sup> lower extremity function,<sup>5-8</sup> and quadriceps muscle performance.<sup>41,42</sup> Furthermore, risk factors for the injury may not be addressed by treatment, which may predispose these athletes to re-injury or act as a barrier to complete recovery.<sup>43-45</sup> Therefore, the goal of this dissertation work was to optimize outcomes of patellar tendinopathy treatment using a comprehensive approach to tendon health, which not only evaluates pain but also other domains of tendon health.

## **6.1 Aim 1: Identify potential modifiable risk factors and modifiable factors associated with patellar tendinopathy through a systematic review and meta-analysis of current literature.**

The purpose of this aim was to conduct a systematic review and meta-analysis of potential modifiable risk factors and associated modifiable factors for patellar tendinopathy. A prior systematic review of patellar tendinopathy risk factors concluded that the vast majority of proposed risk factors had not been prospectively investigated, had limited support from low-quality studies, and/or had conflicting evidence.<sup>44</sup> Additionally, not all risk factors were modifiable, thus, they had limited clinical utility.<sup>44</sup> In the intervening decade since that systematic review was published, there has been an exponential increase in studies investigating potential risk factors for patellar tendinopathy. These new studies may assist in identifying new risk factors or provide additional evidence for proposed risk factors with mixed or limited supporting evidence. Identification of modifiable risk factors and associated modifiable factors for patellar tendinopathy may provide new avenues of treatment and ultimately, improve outcomes by reducing the risk of re-injury.

### **6.1.1 Aim 1.1: Identify potential modifiable risk factors for patellar tendinopathy.**

There was limited or conflicting evidence that decreased ankle dorsiflexion range-of-motion, decreased posterior thigh and quadriceps flexibility, greater volume of jump training, more volleyball sets played per week, greater CMJ height, and greater activity volume are potential modifiable risk factors for patellar tendinopathy.

### **6.1.2 Aim 1.2: Identify modifiable factors associated with patellar tendinopathy.**

There was moderate to conflicting evidence supporting greater volume of strength training, better jumping performance, less normalized hip extension torque,

decreased knee extension fatigue ratio, and altered corticospinal excitability to the quadriceps as associated modifiable factors

## **6.2 Aim 2: Establish stability and reliability of cSWE to evaluate the mechanical properties of the patellar tendon.**

The purpose of this aim was to evaluate the stability and reliability of cSWE to evaluate the mechanical properties of the patellar tendon. Exercise therapy is the treatment with the highest level of evidence for patellar tendinopathy and the success of this intervention is dependent on appropriate load prescription.<sup>13,14</sup> Appropriate loading results in tendon remodeling<sup>19,20,25</sup> and a reduction in symptoms.<sup>16,17,18-24</sup> Unfortunately, determining the correct dosage of tendon loads is challenging, since we have lacked responsive measures of tendon health and remodeling. Pain has been traditionally used to guide load prescription but pain is a poor measure of tendon remodeling.<sup>83</sup> B-mode ultrasound imaging has also been used as a marker of remodeling<sup>89</sup> but changes in tendon structure occur too slowly to be of use in load prescription.<sup>20,89,90</sup> Our research group has developed a form of ultrasound imaging called continuous shear wave elastography (cSWE) which has the ability to measure tendon mechanical properties in-vivo.<sup>91</sup> Mechanical properties may be a more responsive measure of tendon health and remodeling.<sup>91,92</sup> Establishing the reliability and stability of this method may lead to clinical applications, such as monitoring tendon mechanical properties to dose load prescription. This will allow clinicians to better tailor loads to individual patients.

**6.2.1 Hypothesis 2.1: Intra- and inter-rater reliability for shear modulus and viscosity will be moderate to good (ICC  $\geq$  0.6-0.75).**

This hypothesis was partially supported. Intra-rater reliability was moderate for shear modulus (ICC = 0.664 – 0.742) and good for viscosity (0.874 – 0.877). Additionally, inter-rater reliability for viscosity was moderate to good (0.733 – 0.872). However, inter-rater reliability for shear modulus was poor to moderate (0.220 – 0.682), with lower reliability values observed for the most symptomatic limb.

**6.2.2 Hypothesis 2.2: Between days stability for shear modulus and viscosity will be good (ICC  $\geq$  0.5).**

This hypothesis was supported, as ICCs for between-days stability were good for shear modulus (ICC = 0.564 – 0.610) and good to excellent for viscosity (0.760 – 0.933).

**6.2.3 Hypothesis 2.3: Smallest detectable change (SDC) values at the group level for mechanical properties will be less than or equal to values reported for the Achilles tendon (static shear modulus  $\leq$  6.0 kPa and viscosity  $\leq$  3.8 Pa\*s).**

This hypothesis was partially supported. Group level SDC values were equal to or smaller than those reported for the Achilles tendon for viscosity (SDC = 1.1 – 3.8 Pa\*s). However, SDC values for shear modulus were higher than those reported for the Achilles tendon (SDC = 10.8 – 16.3).

**6.3 Aim 3: Explore the relationships between patellar tendon structure (tendon morphology and mechanical properties) and symptom severity (Victorian Institute of Sport Assessment – Patellar questionnaire), lower extremity function (counter-movement jump and drop counter movement jump height) and quadriceps muscle performance (knee extension peak force and quadriceps central activation ratio) in individuals with patellar tendinopathy.**

The purpose of this aim was to explore relationships between altered patellar tendon structure and symptom severity, lower extremity function and quadriceps muscle performance. It has previously been demonstrated that changes in Achilles tendon structure contribute to alterations in other areas of tendon health.<sup>29</sup> This supports the premise that treatment for tendinopathy should aim to normalize tendon structure, as well as reduce symptoms. However, the clinical relevance of tendon structural changes continues to be extensively debated.<sup>83,102,194</sup> In patellar tendinopathy, the contribution of tendon structure to alterations in other domains of tendon health has been marginally investigated but results are conflicting.<sup>25,35,107–110,40,41,101–106</sup> Identifying the role of altered tendon structure in tendon health may help explain the presence of clinical impairments. In turn, this may lead to more targeted treatments that resolve these impairments by addressing alterations in tendon structure.

**6.3.1 Hypothesis 3.1: Tendon morphology (thickness and cross-sectional area) will not relate to symptom severity, lower extremity function but will relate to quadriceps muscle performance.**

**6.3.1.1 Hypothesis 3.1a: There will be no significant relationship between tendon morphology and symptom severity.**

This hypothesis was supported. No significant relationships were observed between tendon morphology and symptom severity (VISA-P scores) after adjusting for age, sex, and BMI ( $p = 0.81$ ,  $R^2$  change = 0.012).

**6.3.1.2 Hypothesis 3.1b: There will be no significant relationship between tendon morphology and lower extremity function.**

This hypothesis was partially supported. There was a significant positive relationship between counter-movement jump (CMJ) height and tendon thickness ( $p < 0.001$ ,  $\beta = 0.718$ ) and a significant negative relationship between CMJ height and tendon CSA ( $p = 0.001$ ,  $\beta = -0.538$ ). However, there was not a significant relationship between drop CMJ height and tendon morphology ( $p = 0.42$ ,  $R^2$  change = 0.037).

**6.3.1.3 Hypothesis 3.1c: Tendon thickness and cross-sectional area will negatively relate to peak knee extension force but not quadriceps central activation ratio.**

This hypothesis was partially supported. There was not a significant relationship between knee extension MVIC force and tendon morphology ( $p = 0.27$ ,  $R^2$  change = 0.11). As expected, there was no significant relationship between quadriceps central activation ratio (CAR) and tendon thickness ( $p = 0.38$ ,  $\beta = 0.214$ ). However, in contrast to what was expected, there was a significant negative relationship between CAR and tendon CSA ( $p = 0.04$ ,  $\beta = -0.517$ ).

**6.3.2 Hypothesis 3.2: Tendon mechanical properties will relate to symptom severity, lower extremity function and quadriceps muscle performance.**

**6.3.2.1 Hypothesis 3.2a: Tendon mechanical properties (static shear modulus and viscosity) will positively relate to symptom severity.**

This hypothesis was not supported. There was no relationship between symptom severity and tendon mechanical properties ( $p = 0.19$ ,  $R^2$  change = 0.099).

**6.3.2.2 Hypothesis 3.2b: Tendon mechanical properties will negatively relate to lower extremity function.**

This hypothesis was not supported. There was a significant positive relationship between CMJ height and viscosity ( $p = 0.006$ ,  $\beta = 0.496$ ) but no relationship between CMJ height and shear modulus ( $p = 0.09$ ,  $\beta = -0.278$ ). Additionally, there was no significant relationship between drop CMJ height and tendon mechanical properties ( $p = 0.39$ ,  $R^2$  change = 0.040).

**6.3.2.3 Hypothesis 3.2c: Tendon mechanical properties will negatively relate to quadriceps muscle performance.**

This hypothesis was not supported. There was no significant relationship between knee extension MVIC force or CAR and tendon mechanical properties,  $p = 0.24$ ,  $R^2$  change = 0.12 and  $p = 0.83$ ,  $R^2$  change = 0.01, respectively.

**6.4 Aim 4: Determine if it is feasible to conduct a randomized clinical trial utilizing pain-guided activity modification during treatment for patellar tendinopathy.**

The purpose of this aim was to examine the feasibility of a randomized clinical trial utilizing pain-guided activity modification during treatment for patellar tendinopathy. Patellar tendinopathy is an overuse injury.<sup>112</sup> Therefore, activity modification is considered a critical component of patellar tendinopathy treatment.<sup>2</sup> Currently, there are not clear guidelines on the extent to which patients with patellar tendinopathy should modify their activity. In studies utilizing exercise therapy to treat patellar tendinopathy, recommendations have ranged from complete cessation of sports activity<sup>21,22,24</sup> to continued activity at the pre-injury level.<sup>17,18,82</sup> Additionally, either of these extremes may have negative consequences. Absence from sport due to injury is associated with negative psychological states<sup>114</sup> and activity cessation may

reduce the tendon's tolerance to sport specific loading. On the other hand, the benefits of exercise therapy may be reduced or nullified by full participation.<sup>82</sup> Pain-guided activity modification may provide a middle-ground, which limits negative psychological consequences of injury, maintains physical readiness for sport, and maximizes recovery.<sup>115,258</sup> However, the impact of pain-guided activity modification on treatment outcomes has not been directly investigated or compared with other forms of activity modification. Prior to conducting a clinical trial to investigate the impact of pain-guided activity modification and compare these impacts with other approaches, it is critical to establish the feasibility of such a study.<sup>116</sup> Ultimately, this aim may lead to a larger clinical trial, which will clarify activity modification recommendations, leading to improved tendon recovery and treatment outcomes.

**6.4.1 Aim 4.1: Examine access to potential participants, percentage of potential participants meeting inclusion criteria, percentage of eligible participants that are willing to be randomized, monthly recruitment and retention.**

One hundred and eight individuals expressed interest in the study over an approximately 13-month recruitment window. Of these individuals, 43.5% were eligible and 31.9% of eligible individuals were willing to be randomized. The recruitment rate was slightly above 1 participant per month (1.15 participants/month). However, the recruitment accelerated in the later stages of the study. The recruitment rate was 0.7 participants per month over the first nine months and 2.25 participants per month over the final four months. Retention was high, with only one missed evaluation session. Overall, 97.7% (44/45) evaluation sessions were completed and one participant was lost to follow-up.

#### **6.4.2 Aim 4.2: Examine the compliance of participants with treatment, activity modification and training diaries.**

The mean±SD compliance with treatment, activity modification, and training diaries for the pain-guided activity group was 86.1±13.0%, 97.3±3.9%, and 98.4±2.7%, respectively. The mean±SD compliance with treatment, activity modification, and training diaries for the pain-free activity group was 67.1±30.7%, 80.2±39.8%, and 81.3±40.0%, respectively.

#### **6.4.3 Hypothesis 4.1: Symptom severity, degree of altered tendon mechanical properties, lower extremity function, and quadriceps muscle performance, but not tendon morphology, will improve significantly in both groups.**

Due to limitations in sample size, the change in outcome measures was analyzed for the total sample, rather than within groups. This hypothesis was partially supported. Symptom severity (VISA-P) significantly improved from baseline to 6-weeks ( $p = 0.043$ , mean difference = 9.2 points) and 12-weeks ( $p = 0.001$ , mean difference = 16.0 points). Mechanical properties did not change significantly over the course of treatment (shear modulus:  $F = 0.512$ ,  $p = 0.606$ ; viscosity:  $F = 0.771$ ,  $p = 0.476$ ). Lower extremity function improved for CMJ height from baseline to 6-weeks ( $p = 0.033$ , mean difference = 1.2 cm) and 12-weeks ( $p = 0.045$ , mean difference = 1.6 cm). However, drop CMJ height did not change significantly over the course of treatment ( $F = 0.370$ ,  $p = 0.695$ ). Additionally, quadriceps muscle performance did not change significantly over the course of treatment (MVIC:  $F = 2.068$ ,  $p = 0.150$ ; CAR:  $F = 1.787$ ,  $p = 0.199$ ). As expected, tendon morphology did not change significantly over the course of treatment (thickness:  $F = 0.618$ ,  $p = 0.549$ ; CSA:  $F = 0.579$ ,  $p = 0.570$ ).

## **6.5 Limitations**

The primary limitation of this work is the small sample sizes for included studies (Aims 2-4). This was due in part to equipment failure, examiner error, and the COVID-19 pandemic halting recruitment and follow-up evaluations. As a result, for Aim 2, the confidence intervals are relatively large around point estimates of reliability and stability. Furthermore, for Aims 3 and 4, we may have been underpowered to detect relationships or changes in outcome measures, respectively. Another limitation was the high heterogeneity between studies included in the meta-analyses in Aim 1. This was partially mitigated by utilizing a random-effects model, which provides a more conservative estimate of effect sizes.<sup>127</sup> However, there is still a risk that the observed effects are due to differences in study design or populations evaluated, rather than true differences in the outcome variable of interest. Finally, a limitation of Aim 3 was the cross-sectional design and lack of a control group consisting of individuals without patellar tendon injury. Without these components, we cannot determine which relationships were influenced by pathological changes in patellar tendon structure.

## **6.6 Conclusions and Clinical Significance**

With patellar tendinopathy, the primary concern of patients and clinicians is pain. Patients want to reduce pain so they can return to activity and clinicians utilize pain as the metric for success with treatment. However, as this work has illustrated, patellar tendinopathy is a wide-reaching injury that impacts multiple domains of tendon health. Furthermore, resolution of pain does not ensure full recovery of tendon health.<sup>28,29</sup> Thus, persisting impairments in other domains of tendon health may be a barrier to complete recovery and predispose athletes to re-injury.

A more comprehensive approach to tendon health is necessary to optimize treatment outcomes for patients with patellar tendinopathy. In the first aim, this work identified potential modifiable risk factors and associated modifiable factors for patellar tendinopathy, including greater volume of activity and sport specific training, greater jumping ability, limited ankle, hip and knee flexibility, decreased hip extension strength and alterations in quadriceps performance. Only quadriceps performance would be addressed by most tendon loading programs, which highlights the importance of evaluating for and addressing impairments throughout the lower extremity and including activity modification as a component of prevention and treatment programs. In the second aim, this work established the reliability and stability of cSWE at the patellar tendon in patients with patellar tendinopathy. This opens the door for use of cSWE in clinical research, which may identify new metrics for tracking the response to tendon loading and eventually lead to more individualized load and recovery prescription. The third aim explored relationships between tendon structure and other domains of tendon health. In this study, relationships were identified between tendon structure and lower extremity function and quadriceps muscle performance. This suggests that it may be necessary to monitor and address tendon structure, even if pain has resolved, to return these athletes back to their pre-injury level of sports performance. Finally, the fourth aim investigated the feasibility of utilizing pain-guided activity modification during treatment for patellar tendinopathy. This study reinforced that individuals with patellar tendinopathy have a host of impairments beyond pain. Furthermore, it set the stage for a larger, more stringent RCT, which may lead to improved activity modification recommendations that balance the need for recovery with the physical and emotional health of athletes.

## **6.7 Future Directions**

This work is only a stepping stone towards utilizing a more comprehensive approach to tendon health and recovery in patellar tendinopathy. However, it does highlight areas that should be prioritized for future research. First, additional prospective studies are needed that follow a cohort of healthy jumping athletes through the development of injury, utilizing this comprehensive model of tendon health. This will help confirm potential risk factors and provide additional information on how various metrics of tendon health are altered by injury. Furthermore, this study design may help clarify whether changes in tendon structure are truly driving impairments in other areas of tendon health, or if they are simply related. Second, now that the stability and reliability of cSWE is established, it is important to investigate how the unique mechanical properties provided by this system respond temporally to varying magnitudes of loading and recovery. Ultimately, this may allow clinicians to fine tune load and recovery prescription to individual athletes. Finally, building upon the pilot and feasibility RCT, a larger, rigorous trial should be conducted using similar methods. This will provide clinicians with evidence-based recommendations for activity modification and broaden our understanding of how the domains of tendon health respond to treatment.

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## Appendix A

### REGRESSION ANALYSIS FOR AIM 3 PRIOR TO OUTLIER REMOVAL

Table A.1: Regression analysis for VISA-P with mechanical properties as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.211	0.303	-0.136	0.491	-0.147	0.312	-0.095	0.641
Sex	-8.822	6.511	-0.257	0.185	-9.258	6.434	-0.269	0.161
BMI	0.344	0.780	0.092	0.670	0.141	0.829	0.038	0.866
Shear Modulus					-0.290	0.173	-0.320	0.104
Viscosity					0.283	0.380	0.151	0.462
<b>R<sup>2</sup></b>		0.094				0.174		
<b>F for change in R<sup>2</sup></b>		1.03				1.408		

BMI = body mass index

Table A.2: Regression analysis for counter-movement jump height with morphology as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.144	0.071	-0.313	0.053	-0.115	0.073	-0.251	0.128
Sex	-5.642	1.393	-0.568	<b>&lt;0.001</b>	-4.936	1.445	-0.497	<b>0.002</b>
BMI	-0.291	0.169	-0.274	0.095	-0.309	0.169	-0.291	0.079
Pain	0.364	0.324	0.154	0.271	0.432	0.354	0.183	0.232
Thickness					6.894	4.260	0.320	0.117
CSA					-2.371	2.308	-0.208	0.314
R <sup>2</sup>			0.472				0.519	
F for change in R <sup>2</sup>			<b>6.473</b>				1.314	

BMI = body mass index; CSA = cross-sectional area.

Table A.3: Regression analysis for drop counter-movement jump height with mechanical properties as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.044	0.158	-0.049	0.785	-0.034	0.155	-0.039	0.828
Sex	-7.704	1.907	-0.699	<b>&lt;0.001</b>	-7.853	1.874	-0.713	<b>&lt;0.001</b>
BMI	-0.407	0.274	-0.303	0.151	-0.463	0.276	-0.345	0.109
Pain	-0.555	0.485	-0.180	0.265	-0.434	0.482	-0.141	0.378
Shear Modulus					-0.056	0.052	-0.192	0.296
Viscosity					0.170	0.100	0.300	0.105
R <sup>2</sup>			0.472				0.537	
F for change in R <sup>2</sup>			<b>5.135</b>				1.478	

BMI = body mass index.

Table A.4: Regression analysis for MVIC force with morphology as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>
<b>Age</b>	-4.551	8.428	-0.144	0.597	-2.335	8.451	-0.074	0.786
<b>Sex</b>	73.388	145.403	0.131	0.621	147.821	157.227	0.263	0.363
<b>BMI</b>	6.450	15.414	0.118	0.681	10.276	16.229	0.188	0.537
<b>Pain</b>	-38.694	24.258	-0.380	0.130	-48.213	26.809	-0.474	0.094
<b>Thickness</b>					562.077	498.616	0.436	0.279
<b>CSA</b>					-364.640	218.303	-0.545	0.117
<b>R<sup>2</sup></b>		0.143				0.286		
<b>F for change in R<sup>2</sup></b>		0.670				1.399		

BMI = body mass index; CSA = cross-sectional area.

Table A.5: Regression analysis for MVIC force with mechanical properties as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>P-value</i>
<b>Age</b>	-4.959	9.539	-0.163	0.611	-3.681	9.965	-0.121	0.718
<b>Sex</b>	25.608	163.355	0.044	0.878	63.695	175.895	0.108	0.723
<b>BMI</b>	4.541	16.340	0.088	0.785	3.904	17.296	0.0753	0.825
<b>Pain</b>	-39.711	23.172	-0.443	0.107	-38.569	24.501	-0.430	0.140
<b>Shear Modulus</b>					1.608	4.202	0.118	0.708
<b>Viscosity</b>					5.140	8.684	0.195	0.564
<b>R<sup>2</sup></b>		0.168				0.238		
<b>F for change in R<sup>2</sup></b>		0.759				0.590		

BMI = body mass index.

Table A.6: Regression analysis for CAR with morphology as predictor variables prior to removal of outliers.

Variable	Model 1				Model 2			
	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>	<i>B</i>	<i>SE B</i>	$\beta$	<i>p-value</i>
Age	-0.226	0.390	-0.118	0.571	-0.167	0.354	-0.087	0.645
Sex	16.308	6.731	0.481	<b>0.028</b>	18.135	6.578	0.535	<b>0.015</b>
BMI	0.844	0.714	0.256	0.254	1.333	0.679	0.405	0.070
Pain	-3.738	1.123	-0.610	<b>0.004</b>	-3.747	1.122	-0.611	<b>0.005</b>
Thickness					14.609	20.862	0.188	0.495
CSA					-21.302	9.127	-0.528	<b>0.035</b>
<b>R<sup>2</sup></b>			0.495				0.656	
<b>F for change in R<sup>2</sup></b>			<b>3.916</b>				3.280	

CAR = central activation ratio; BMI = body mass index; CSA = cross-sectional area.

## **Appendix B**

### **RECRUITMENT STRATEGY FOR PILOT AND FEASIBILITY STUDY**

The recruitment strategy was developed to reach a wide audience through a variety of media formats to ensure a representative sample of participants with patellar tendinopathy. Beginning in January, 2019, local orthopedic and sports medicine physicians, as well as the University of Delaware Physical Therapy clinic, were notified of study initiation and provided with consent to contact forms and study flyers. The flyers directed interested individuals to an online REDCap survey where they could submit contact information and answer preliminary screening questions. On February 26<sup>th</sup>, 2019, additional flyers were posted in athletic centers and gyms throughout New Castle County, DE. Facebook and Instagram advertisements were begun on May 9<sup>th</sup>, 2019, with a target audience of sports medicine professionals, coaches, and adults within the target age range with interests in sports or recreational fitness. On September 1<sup>st</sup>, 2019, advertisements were initiated with Delaware Sports League, an adult recreational sports league. These advertisements included monthly emails and dedicated social media posts. Delaware Sports League advertisements ran from September through November. The total number of interested individuals and the outcomes of screening are displayed in Figure A.1.

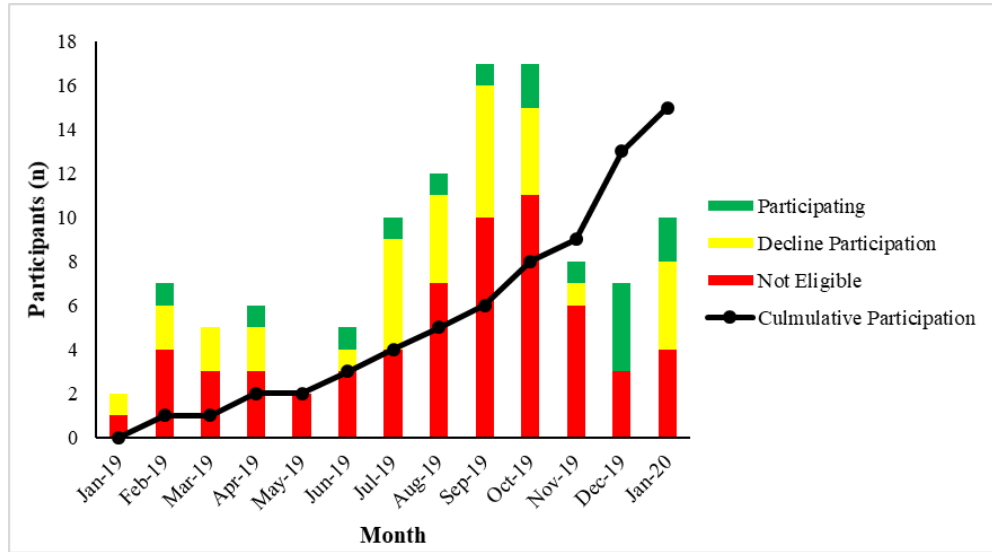


Figure B.1: Recruitment by month for pilot and feasibility randomized clinical trial.

## Appendix C

### TRAINING DIARY UTILIZED IN AIM 4

Date	Home exercises (include which exercise, reps, sets and load)	Running or Jumping	Physical activity	Pain level 0-10 0 = No Pain 10 = Worst Pain Imaginable
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____
		YES / NO		Morning: _____ Before Activity: _____ During Activity: _____ After Activity: _____

Figure C.1: Training diary utilized in Aim 4.

## Appendix D

### MODIFIED HEAVY-SLOW RESISTANCE PROGRAM USING RESISTANCE BANDS




 <p><b>Banded Squat</b></p> <ol style="list-style-type: none"><li>1) Stand with both feet on the band and squat down until you are able to loop the band over your shoulders and the back of your neck. Do NOT position band so that runs in front of your neck. Stabilize the band by gripping it in your hands with the palms facing forward.</li><li>2) Position the feet shoulder width apart.</li><li>3) Return to the standing position.</li><li>4) Squat down by pushing the hips backwards and bending at the knees until the thighs are parallel with the floor. Throughout the motion, keep the back neutral, the chest up, and the heels on the floor.</li><li>5) Return to the starting position.</li></ol> <p>Perform the exercise in a slow and controlled manner. Each repetition should take 6 seconds total (3 seconds down, 3 seconds up). Difficulty can be increased/decreased by widening/narrowing your grip or changing the band being used.</p>	 <p><b>Banded Knee Extension</b></p> <ol style="list-style-type: none"><li>1) In a seated position, loop the band around your ankles. Due to the length of the bands, you may need to loop it multiple times. Alternatively, the band may be looped around a sturdy structure and the leg being used for the exercise may be placed in the loop.</li><li>2) Begin with the knees flexed to 90 degrees, as shown in the picture.</li><li>3) Straighten the knees as far as possible. NOTE: Since the resistance increases the more you straighten your knee, you may not be able to fully extend the leg.</li><li>4) Return to the starting position.</li></ol> <p>Perform the exercise in a slow and controlled manner. Each repetition should take 6 seconds total (3 seconds up, 3 seconds down).</p>
 <p><b>Banded Leg Press</b></p> <ol style="list-style-type: none"><li>1) Position the band so it runs behind your back, just above or below your shoulder blades. Lie on your back and bring your knees to your chest. Loop the band around one or both feet. Due to the length of the band, you may need to loop it multiple times around your foot/feet.</li><li>2) Begin with the knees flexed to 90 degrees, as shown in the picture.</li><li>3) Straighten the knees until the legs are completely straight, or as close to straight as the resistance of the band will allow.</li><li>4) Return to the starting position.</li></ol> <p>Perform the exercise in a slow and controlled manner. Each repetition should take 6 seconds total (3 seconds up, 3 seconds down).</p>	

Figure D.1: Modified Heavy-Slow Resistance protocol.

## Appendix E

### RELIABILITY AND RESPONSIVENESS OF OUTCOME MEASURES

Table E.1: Reliability and responsiveness of outcome measures.

	ICC	SEM	SDC <sub>95%-</sub> individual	SDC <sub>95%-</sub> group	MCID
<b>VISA-P (points)</b> <sup>261</sup>	0.95	4.0	11.1	1.2	13.0
<b>TSK-17 (points)</b> <sup>290,291</sup>	0.91	3.3	9.2	0.7	N.E.
<b>DASS-21 (points)</b> <sup>292</sup>	N.E.	N.E.	10.12	0.26	N.E.
<b>Tendon Thickness (mm)</b> <sup>177</sup>	0.82 - 0.96	0.21	0.59	0.16	N.E.
<b>Tendon CSA (mm<sup>2</sup>)</b>	0.878 – 0.882	11.2	31.0	11.7	N.E.
<b>Static Shear Modulus (kPa)</b>	0.664 – 0.742	14.1 – 21.1	39.1 – 58.6	10.8 – 16.3	N.E.
<b>Viscosity (Pa*sec)</b>	0.874 – 0.877	1.4 – 4.9	3.8 – 13.6	1.1 – 3.8	N.E.
<b>CMJ Height (cm)</b> <sup>196</sup>	0.91	1.44	3.99	0.73	N.E.
<b>Drop CMJ Height (cm)</b> <sup>196</sup>	0.88 – 0.92	1.66	4.61	0.84	N.E.
<b>Knee Extension MVIC (% change)</b> <sup>275</sup>	0.98	5.67	15.72	2.87	N.E.
<b>Quadriceps CAR (%)</b> <sup>270</sup>	0.97	2.36	6.55	2.07	N.E.

ICC = Intraclass correlation coefficient, SEM = Standard error of measure, SDC = Smallest detectable change, MCID = Minimally clinically important difference, VISA-P = Victorian Institute of Sport Assessment – Patellar Tendon questionnaire, TSK = Tampa Scale of Kinesiophobia, CSA = Cross-sectional area, CMJ = Counter-movement jump, MVIC = Maximum voluntary isometric contraction, CAR = Central activation ratio, N.E. = Not established

## Appendix F

### RESULTS OF GENERALIZED LINEAR MIXED MODEL FOR OUTCOME MEASURES IN AIM 4

Table F.1: Effects of group and time of generalized linear mixed model for outcome measures in Aim 4 after outlier removal.

Category	Outcome	Time		Group	
		F	p	F	p
<b>Symptoms</b>	VISA-P	6.587	<b>0.005</b>	6.064	<b>0.029</b>
<b>Psychological Factors</b>	TSK	3.528	<b>0.045</b>	1.428	0.253
	DASS-21	2.800	0.081	6.678	<b>0.005</b>
<b>Morphology</b>	Thickness	0.618	0.549	0.074	0.790
	CSA	0.579	0.570	0.403	0.536
<b>Mechanical Properties</b>	Shear Modulus	0.512	0.606	0.487	0.496
	Viscosity	0.771	0.476	0.109	0.746
<b>Lower Extremity Function</b>	CMJ Height	3.608	<b>0.046</b>	0.011	0.918
	Drop CMJ Height	0.370	0.695	0.125	0.729
<b>Quadriceps Muscle Performance</b>	MVIC	2.068	0.150	3.743	0.078
	CAR	1.787	0.199	3.326	0.099

CSA = cross-sectional area; CMJ = counter-movement jump; MVIC = maximal voluntary isometric contraction; CAR = central activation ratio.

Table F.2: Effects of group and time of generalized linear mixed model for outcome measures in Aim 4 prior to outlier removal.

Category	Outcome	Time		Group	
		F	p	F	p
<b>Symptoms</b>	VISA-P	6.587	<b>0.005</b>	6.064	<b>0.029</b>
<b>Psychological Factors</b>	TSK	3.528	<b>0.045</b>	1.428	0.253
	DASS-21	2.806	0.079	0.581	0.459
<b>Morphology</b>	Thickness	0.618	0.549	0.074	0.790
	CSA	0.229	0.797	0.220	0.647
<b>Mechanical Properties</b>	Shear Modulus	0.512	0.606	0.487	0.496
	Viscosity	0.771	0.476	0.109	0.746
<b>Lower Extremity Function</b>	CMJ Height	3.608	<b>0.046</b>	0.011	0.918
	Drop CMJ Height	0.370	0.695	0.125	0.729
<b>Quadriceps Muscle Performance</b>	MVIC	2.068	0.150	3.743	0.078
	CAR	1.787	0.199	3.326	0.099

CSA = cross-sectional area; CMJ = counter-movement jump; MVIC = maximal voluntary isometric contraction; CAR = central activation ratio.

Table F.3: Estimated marginal means, standard error and pair-wise comparisons of timepoints for the pooled sample prior to outlier removal.

Category	Outcome	Baseline		6-Weeks		12-Weeks		p-values		
		M	SE	M	SE	M	SE	Baseline to 6-Weeks	Baseline to 12-Weeks	6-Weeks to 12-Weeks
<b>Symptoms</b>	VISA-P (points)	59.6	3.8	68.8	3.8	75.6	4.0	<b>0.043</b>	<b>0.001</b>	0.136
<b>Psychological Factors</b>	TSK (points)	36.4	1.1	35.8	1.1	34.2	1.1	0.448	<b>0.015</b>	0.075
	DASS-21 (points)	3.2	1.4	4.3	1.4	6.2	1.4	0.383	0.027	0.146
<b>Morphology</b>	Thickness (mm)	6.9	0.5	6.8	0.5	6.6	0.6	0.427	0.329	0.678
	CSA (mm <sup>2</sup> )	115.3	10.8	118.0	10.8	119.7	12.0	0.613	0.558	0.821
<b>Mechanical</b>	Shear Modulus (kPa)	70.6	6.3	77.1	6.2	79.8	9.2	0.427	0.391	0.796
	Viscosity (Pa*sec)	31.6	2.4	29.7	2.3	33.0	3.1	0.396	0.628	0.268
<b>Lower Extremity Function</b>	CMJ Height (cm)	12.1	1.2	13.3	1.2	13.7	1.3	<b>0.033</b>	<b>0.045</b>	0.620
	Drop CMJ Height (cm)	13.4	1.2	13.9	1.3	13.4	1.4	0.423	0.953	0.588
<b>Quadriceps Muscle Performance</b>	MVIC (N)	860.9	56.7	995.9	60.0	1053.4	85.6	0.138	0.082	0.601
	CAR (%)	80.6	3.3	84.1	3.8	90.7	4.9	0.440	0.076	0.250

CSA = cross-sectional area; CMJ = counter-movement jump; MVIC = maximal voluntary isometric contraction; CAR = central activation ratio

## Appendix G

### IRB/HUMAN SUBJECTS APPROVAL



Institutional Review Board  
210H HULLIHEN HALL  
NEWARK, DE 19716  
PHONE: 302-831-2137  
FAX: 302-831-2828

DATE: July 10, 2019

TO: Karin Silbernagel, PT, PhD, ATC  
FROM: University of Delaware IRB

STUDY TITLE: [1450331-1] Reliability of Continuous Shear Wave Elastography (cSWE) at the Patellar Tendon

SUBMISSION TYPE: New Project

ACTION: APPROVED

EFFECTIVE DATE: July 10, 2019

NEXT REPORT DUE: July 9, 2020

REVIEW TYPE: Expedited Review

REVIEW CATEGORY: Expedited review category # (4,7)

Thank you for your New Project submission to the University of Delaware Institutional Review Board (UD IRB). The UD IRB has reviewed and APPROVED the proposed research and submitted documents via Expedited Review in compliance with the pertinent federal regulations.

As the Principal Investigator for this study, you are responsible for, and agree that:

- All research must be conducted in accordance with the protocol and all other study forms as approved in this submission. Any revisions to the approved study procedures or documents must be reviewed and approved by the IRB prior to their implementation. Please use the UD amendment form to request the review of any changes to approved study procedures or documents.
- Informed consent is a process that must allow prospective participants sufficient opportunity to discuss and consider whether to participate. IRB-approved and stamped consent documents must be used when enrolling participants and a written copy shall be given to the person signing the informed consent form.
- Unanticipated problems, serious adverse events involving risk to participants, and all non-compliance issues must be reported to this office in a timely fashion according with the UD requirements for reportable events. All sponsor reporting requirements must also be followed.

The UD IRB REQUIRES the submission of a PROGRESS REPORT DUE ON July 9, 2020. A continuing review/progress report form must be submitted to the UD IRB at least 45 days prior to the due date to allow for the review of that report.

If you have any questions, please contact the UD IRB Office at (302) 831-2137 or via email at [hsrb-research@udel.edu](mailto:hsrb-research@udel.edu). Please include the study title and reference number in all correspondence with this office.

Figure G.1: Institutional review board approval for Aim 2.



RESEARCH OFFICE

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

DATE: June 2, 2016

TO: Karin Silbernagel, PT, ATC, PhD  
FROM: University of Delaware IRB

STUDY TITLE: [901281-1] Patellar tendinopathy functional, clinical and structural outcomes

SUBMISSION TYPE: New Project

ACTION: APPROVED  
APPROVAL DATE: June 2, 2016  
EXPIRATION DATE: May 17, 2017  
REVIEW TYPE: Full Committee Review

REVIEW CATEGORY: *Research with Children Subpart D Determination 45 CFR 46.404*

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

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

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

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

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

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

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

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

Figure G.2: Institutional review board approval for Aim 3.



RESEARCH OFFICE

210 HULLIHEN HALL  
UNIVERSITY OF DELAWARE  
NEWARK, DELAWARE 19716-155  
PH: 302/831-2136  
FAX: 302/831-2828

DATE: May 7, 2018

TO: Karin Silbernagel, PT, ATC, PhD  
FROM: University of Delaware IRB

STUDY TITLE: [1217479-1] Continued Activity During Rehabilitation in Patients with Patellar Tendinopathy

SUBMISSION TYPE: New Project

ACTION: APPROVED  
APPROVAL DATE: May 7, 2018  
EXPIRATION DATE: April 17, 2019  
REVIEW TYPE: Full Committee Review

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

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

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

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

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

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

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

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

Figure G.3: Institutional review board approval for Aims 3 and 4.

**Appendix H**  
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