Chapter 1

General Introduction
Jumper’s knee: A patient’s story

Last year I moved from a team that plays at the regional level to one that plays at the national level. I went from training twice a week to training four times a week and also started with strength training. The training sessions of my new team were more intensive than the sessions I was used to. Besides playing volleyball I am also a university student and work two nights as a waiter in a restaurant. After playing for two months for my new team my knee became painful. The pain was located just below the kneecap. At first the pain was only present during warm-ups and after playing volleyball. After a while the pain was also present during games and it became impossible to play, so I rested for a month. Then I tried to start again with training, but the pain recurred. At this point I went to see my GP. He told me I had a jumper’s knee and prescribed rest, NSAIDS and physical therapy. The physical therapist instructed me to perform eccentric exercises and after two months I was able to do decline squats without pain. I then decided to restart volleyball training, but again the pain recurred. As a result of this I missed the last part of the volleyball season. During the summer break symptoms diminished and at the beginning of the new season I was fully involved in the training sessions. After five weeks the pain came back, so I went to see my GP again. He gave me an injection with corticosteroids, which enabled me to train and play without pain. A few weeks later the pain returned and was even worse than before the injection. I am therefore not involved in volleyball at the moment. As long as I refrain from playing volleyball the pain is tolerable, but I would like to play again. I have searched the internet and talked to teammates, and several treatment options that include all kinds of injections, shockwave therapy and surgery are recommended. I am desperate as to what to do. Hey doctor, why did I get this bothersome injury and which treatment is going to be effective to get me to play again?

Introduction

Patellar tendinopathy (also called jumper’s knee) is an injury that is characterised by activity-related pain in the patellar tendon, typically located proximally in the tendon just below the patella, although it can also be located distally in the tendon.\(^1\) Patellar tendinopathy (PT) is a common injury among jumping athletes. Elite basketball and volleyball players show a prevalence of 30-45 % and recreational players of 10-15%.\(^2,3\) PT is a troublesome injury (see the patient’s story) that may force athletes to end their sports career and can even keep causing mild but long-lasting symptoms after that.\(^4\) Four phases of symptoms and functional impairment
have been described: 1) pain after activity only, 2) pain at the start of activity and after activity, 3) pain during and after activity and inability to compete and 4) total rupture of the tendon.5 These four phases can be distinguished clinically, but the underlying pathology forms a continuum.6

The patellar tendon

The function of a tendon is to transmit contractile forces from the muscle to the skeleton, to produce joint motion. Tendons have a hierarchical structure (figure 1). The smallest entity in a tendon is the microfibril. A group of microfibrils forms a fibril, the smallest structural unit. A group of fibrils in the extracellular matrix forms a fibre and a group of fibres bound together by endotenon forms a fascicle. Most fibres run in parallel with the long axis of the tendon. Fascicles are surrounded by epitendon. The paratenon forms the outer layer of the tendon.7,8

A tendon is mainly composed of Type I collagen, and accounts for 95% of the total collagen. The second most present form of collagen is Type III collagen and is mainly found in the endotenon and epitendon. Type III collagen has less mechanical strength than Type I collagen, because it produces smaller and less organized fibrils.7,8

The patellar tendon has, in contrast to many other tendons, no direct attachment to muscle tissue, but is attached at both ends to the skeleton through an osteotendinous junction. The patellar tendon has fibrocartilaginous insertions to the lower pole of the patella (figure 2A) and the tibial tuberosity (figure 2B). A fibrocartilaginous osteotendinous junction is composed of four zones: tendon, uncalcified fibrocartilage, calcified fibrocartilage and bone.9 The fibrocartilage zones are thought to balance the different elasticity modes of tendon and bone.10 Tendinopathy at the insertion of the quadriceps to the upper pole of the patella is not considered to be jumper’s knee in this thesis and is therefore not addressed.8

Pathophysiology of (patellar) tendinopathy

Patellar tendinopathy used to be called patellar tendinitis and was thought to be an inflammatory condition. However, in the last decade there has been a paradigm shift towards the opinion that (patellar) tendinopathy is mainly a degenerative condition (tendinosis),11 although some believe that inflammation (tendinitis) may play a role in (the early stages of) tendinopathy.12 Because tendinosis can only be confirmed by means of histopathological examination, the term tendinopathy is often used in clinical practice.
Figure 1. The hierarchical structure of a tendon. (Reproduced from Riley, The pathogenesis of tendinopathy: A molecular perspective, Rheumatology, 2004, 43 (2): 131-142, by permission of the British Society for Rheumatology.)

Figure 2. A. Section of the inferior pole of the patella (P), showing the enthesis (E) of the patellar tendon (PT) (HP = Hoffa’s fat pad, T1 and T2 = trabeculae that run in superior inferior and anterior posterior direction). B. Section of the distal enthes (E) of the patellar tendon to the tibial tuberosity (TT) (PF = periostal fibrocartilage, S = synovium, ST = subsynovial tissue). (A: Reproduced from Journal of Anatomy, Toumi et al., 208, 47-57, 2006. B: Reproduced from Arthritis & Rheumatism, Benjamin et al., 50, 3306-3313, 2004, both with permission from John Wiley and Sons.)
Magnusson and Kjaer (2010) have suggested that tendinopathy is caused by a disbalance between the anabolic synthesis and the catabolic breakdown of the collagenous matrix of the tendon. A number of histological changes are found in the pathological tendon. There are changes in cellularity (apoptosis), cell rounding, decreased matrix organisation and infiltration of blood vessels and accompanying nerves (neoneurovascularisations). Besides histological changes there are also biochemical ones. Firstly, changes are found in matrix structure, such as an increase in the amount of type III collagen, and an increase in production of large-molecular proteoglycans such as aggrecan and versican. These proteoglycans bind water and contribute to the swelling of the tendon. Secondly, there are changes in cytokines and signalling factors such as an increase in glutamate, substance P, calcitonin gene-related peptide (CGRP) and vascular endothelial growth factor VEGF (VEGF). And thirdly, changes have been found in concentrations of enzymes such as matrix metalloproteinases (MMPs) and a disintegrin and metalloproteinases (AD-AMs) that play a role in matrix remodelling. These changes, however, do apply to tendinopathy of the main body of the tendon whereas most overuse injuries to the patellar tendon (also) involve the insertion sites where the tendon connects to the bone (osteotendinous junctions). In approximately 85% of the cases the proximal insertion (figure 2A) is affected and in 15% the distal (tibial) insertion (figure 2B). Reasons why the osteotendinous junction is often affected are the low flexibility, the arrangement of fibres in relation to the direction of muscle force, and a small insertion zone compared to muscle size.

The continuum model of tendinopathy distinguishes three phases of tendinopathy that form a continuum (figure 3). The first phase is reactive tendinopathy, characterised by increased tendon thickness as a result of acute overload. The increase in tendon thickness reduces the stress placed on the tendon. There are no changes in collagen integrity in this phase. The second phase is tendon disrepair, which presents greater matrix changes. There is a separation of collagen, a disorganisation of the matrix and an increase in cells. There may also be an increase in vascularity and neuronal ingrowth in the tendon. The last phase is that of degenerative tendinopathy, in which the disorganisation of the matrix is more widespread. Because of acellularity (a result of apoptosis), the matrix is filled with vessels, matrix breakdown products and little collagen. The model presents a continuum with overlap between stages. The last stage, degenerative tendinopathy, is thought to be irreversible. The model is based on clinical, imaging and histopathological knowledge, and does justice to the observation that there are varieties in tendinopathy. The
model is still hypothetical and further research is required to validate it. Several theories have been proposed about what causes tendinopathy. Rees et al. (2009) distinguished three theories that are not mutually exclusive: the mechanical theory, the vascular theory and the neural theory. According to the mechanical theory, micro-injuries in the tendon resulting from overload and a subsequent failed healing process can eventually lead to matrix and cellular changes as well as altered mechanical properties of the tendon. Besides overload, underloading of a tendon can also cause pathology. Another theory, a variant of the mechanical theory and specific for PT, is that the primary cause are compressive loads (caused by impingement) rather than tensile loads. These compressive forces at
the proximal posterior part of the patellar tendon cause histological changes as a result of an adaptive process. This causes more tensile stress to be placed on the surrounding tendon tissue, leading to overload of this tissue. This theory is in line with the finding that the maximal tensile strain is not found at the posterior side of the proximal tendon, which is the most common site for PT. The vascular theory places the cause of tendinopathy in poor blood supply to tendons. This theory addresses mainly the supraspinatus, Achilles and tibialis posterior tendons, which are thought to have certain avascular areas. However, it has been debated whether these avascular areas actually exist. The neural theory suggests that the release of neurotransmitters such as substance P and glutamate may cause pain. These theories are not mutually exclusive and may all explain the pathophysiology of PT to a certain extent, but further research is needed to determine if and how such mechanisms play a role in this pathophysiology.

**Pain in patellar tendinopathy**

It is not clear yet what causes pain in tendinopathy. Early theories suggest that pain is caused either by an inflammatory condition (tendinitis) or by separation of collagen fibres such as in ligament injury. As already discussed, tendinopathy is not considered to be an inflammatory condition, therefore this is unlikely to be the cause of the pain. Furthermore, although injury to the collagen fibres plays a role in the pain associated with tendinopathy it does not explain the pain mechanism completely, because a number of studies have shown that there is no relation between collagen structure and pain. The pain must thus be sought elsewhere, and it has been suggested that biochemical substances, such as glutamate and substance P, may be causing the pain by irritating nociceptors. Neovascularisations (with accompanying nerves) may also play a role in the pain mechanism. In a population of subjects with patellar tendon imaging abnormalities it was shown that persons with neovascularisations in their tendons experienced more pain than those without. Some studies have shown however that these neovascularisations are also present in asymptomatic subjects, while others have shown that neovascularisations are not related to pain in reactive tendinopathy, given that pain precedes them. Somatosensory changes may also explain the pain in PT to a certain extent as it has been found that subjects with PT often show sensitisation, which leads to allodynia (pain due to a stimulus that normally does not cause pain) and hyperalgesia (an increased pain response). PT may already exist for a long time before the onset of symptoms. Also, when symptoms disappear pathology may still
be visible on imaging. This phenomenon is called the ‘iceberg theory’: the pathology is often present below the pain threshold (figure 4).12,30

Etiology and prevention

Since PT causes long-lasting symptoms and may force athletes to give up their sports participation, prevention of this injury is important. Finch (2006) developed a framework for sports injury prevention called TRIPP (Translating Research into Injury Prevention Practice).31 The framework consists of 6 stages (figure 5). According to this framework the first step towards prevention is injury surveillance in order to describe the magnitude of the problem. For PT a number of studies have been published that address this first stage.2,3,32 The second stage of the TRIPP framework is understanding of the etiology of an injury. Research into this stage should focus on risk factors that can be identified in epidemiological studies and injury mechanisms that require biomechanical studies. In the following stages of the TRIPP model (stages 3-6), the knowledge gained in the second stage can be used to develop evidence-based preventive measures. Several studies have addressed
the second stage of the framework and a vast number of possible risk factors has been suggested. This makes it difficult to draw conclusions as to what are the most important risk factors. Also, most research has focused on elite athletes, therefore the second stage of the framework needs to be further addressed.

Management

The diagnosis of PT is a clinical one and is based on a combination of physical examination, history-taking and imaging. A difficulty with imaging is that tendon abnormalities are not always accompanied by symptoms and changes in symptoms do not always correlate with structural changes. The VISA-P questionnaire is often used to assess the severity of PT. It measures pain, function and sport participation in subjects with PT.

Because risk factors are unclear, prevention of PT often fails. For this reason, besides research into these risk factors effective treatment to recover from PT is essential. With the paradigm shift from tendinitis to tendinosis, there has also been a shift away from treatments that focus on anti-inflammation, such as NSAIDs and corticosteroid injections, towards treatments that target the degeneration of tendon tissue. According to Kountouris and Cook (2007), a tendinopathy rehabilitation program should consist of three essential components. The first component is modifying tendon load to diminish symptoms. Although load reduction is important, total rest and unloading of the tendon is not advisable. Activity is thought to be better for regeneration of tendon tissue than inactivity, because inactivity decreases collagen synthesis. Muscle-tendon function as well as pelvic and lower limb kinetic chain function should also be assessed. When the first goal (diminishing symptoms and addressing the kinetic chain, e.g. ankle dorsiflexion range) is reached, there is room to place load on the tendon and to move to the second component: exercise-based rehabilitation and adapting the tendon to increasing load. Eccentric exercises are the most common exercises used in an exercise-based rehabilitation program. They were first introduced to treat mid-portion Achilles tendinopathy. Eccentric exercise may have a positive effect on PT, with a 50-70% chance of improvement. It is not exactly clear why eccentric exercises are effective, but it may be related to high-frequency oscillations in tendon force during the eccentric phase as Rees et al. (2008) showed for the Achilles tendon. The general consensus is that when performing eccentric exercises for PT a decline board should be used, some pain should be experienced, and subjects
should avoid sports activity during the exercise period. A recent study however found heavy slow resistance training, including both a concentric and an eccentric phase, to be more effective in improving symptoms than eccentric exercises. This implies that both the concentric and the eccentric phase may have a positive effect on the tendon. According to Cook it is important to avoid exercises that use the elastic function of the tendon. This indicates that resistance training at low speeds may be beneficial.

The third component of the rehabilitation program outlined by Kountouris and Cook consists of additional treatment options. They mention addressing foot pronation/supination, ankle mobilisation and increasing hamstring and quadriceps flexibility. There are a number of other options described in the literature. One of them is Extracorporeal Shockwave Therapy (ESWT) a non-invasive treatment option for tendinopathy that uses high-pressure waves to generate a mechanical
effect on the tendon tissue. In a review of the literature it was concluded that ESWT is a safe and promising method for treating PT, but that further research was required.\textsuperscript{50} Later it was shown that ESWT is not effective in subjects that have symptoms for less than a year and who continue to participate in their sport.\textsuperscript{51} Another treatment option is the injection of a substance in or around the patellar tendon. A number of substances can be injected, such as, steroids, polidocanol, aprotinin, and platelet rich plasma (PRP). Several studies have been conducted that looked at the effectiveness of these injections yet the necessary scientific evidence is missing in all of them.\textsuperscript{52} Only for steroids is there some evidence for a positive effect on PT in the short term, mainly on pain reduction, but in the long term this effect disappears,\textsuperscript{52} and results may be worse than with most conservative treatments.\textsuperscript{53, 54} Finally, surgery can be an option for treating PT, but results of studies investigating the effectiveness of surgery are also equivocal.\textsuperscript{55-57} In general, it can be concluded that currently there is no definitive treatment for PT available.\textsuperscript{49}

Aims of the thesis

The general objective of this thesis is to improve prevention and treatment of PT. The thesis has two aims. First, to increase knowledge about the etiology of PT. According to the TRIPP model, knowledge of risk factors is essential to develop preventive measures. A large number of risk factors have been suggested, but the literature seems dissimilar and inconclusive. For this reason, the literature on risk factors for PT will be reviewed and risk factors for PT in elite as well as non-elite basketball and volleyball players will be addressed.

ESWT is one of the treatment options for PT. Two types of shockwave devices are available at the moment: focused shockwave and radial shockwave devices. Most basic and clinical studies have used focused shockwave devices, but in the Netherlands radial shockwave devices are used more widely to treat PT.\textsuperscript{58} Because of this discrepancy between science and practice, the second aim is to gain knowledge about ESWT as a treatment for PT, and more specifically about the differences between focused and radial ESWT.

Outline of the thesis

The first part of this thesis is about the etiology of PT. Chapter 2 provides a systematic overview of the literature concerning risk factors for PT. Chapter 3 reviews the literature that examines the relation between jumping biomechanics and PT. The
following chapters exhibit the results of a cross-sectional survey concerning risk factors for PT among basketball and volleyball players (of all playing levels). Chapter 4 describes demographic, anthropometric and sport-related risk factors, and Chapter 5 occupational risk factors. This last chapter also describes the relation between PT and work limitations.

The topic of the second part of this thesis is the treatment of PT, with Chapter 6 giving a practical overview of ESWT as a treatment for tendinopathy and Chapter 7 presenting the design of a Randomized Controlled Trial (RCT) that compares the effectiveness of radial and focused ESWT. The results of this RCT are presented in Chapter 8.

This thesis ends with Chapter 9, which provides a general overview of this thesis and discusses findings as well as suggestions for future research.
References


