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On the causes of patellar tendinopathy

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List of papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals:

I. Lian Ø, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports – A cross-sectional study. Am J Sports Med 33: 561-567, 2005.

II. Lian Ø, Holen K, Engebretsen L, Bahr R. Relationship between symptoms of jumper's knee and the ultrasound characteristics of the patellar tendon among high level male volleyball players. Scand J Med Sci Sports 6: 291-296, 1996.

III. Lian Ø, Engebretsen L, Øvrebø RV, Bahr R. Characteristics of leg extensors in male volleyball players with jumper's knee. Am J Sports Med 24: 380-385, 1996.

IV. Lian Ø, Refsnes PE, Engebretsen L, Bahr R. Performance characteristics of volleyball players with patellar tendinopathy. Am J Sports Med 31: 408-413, 2003.

V. Lian Ø, Dahl J, Ackermann P, Frihagen F, Engebretsen L, Bahr R. Pronociceptive and antinociceptive neuromediators in patellar tendinopathy. Am J Sports Med 34: 1801-1808, 2006.

VI. Lian Ø, Scott A, Engebretsen L, Duronio V, Bahr R, Khan K. Excessive apoptosis in patellar tendinopathy in athletes. Am J Sports Med Epub Jan 23, 2007.

Definitions

Nomenclature. The nomenclature used to characterize different tendon disorders has been confusing, at least in part because of a lack of understanding of the underlying pathology. Based on previous definitions described by Jozsa and Kannus 1997, Clancy 1990, Leadbetter 1992 and Khan et al. 1998 the following terminology is used in this thesis:

Paratenonitis. Previously named "tenosynovitis", "tenovaginitis" and "peritendinitis". This is an inflammation of only the paratenon, either lined by synovium or not. The histopathologic findings consist of inflammatory cells in paratenon or peritendinous areolar tissue. The clinical signs and symptoms include the cardinal inflammatory signs with swelling, pain, crepitation, local tenderness, warmth and dysfunction.

Paratenonitis with tendinosis. Previously named "tendinitis". Characterized by paratenon inflammation associated with intratendinous degeneration. The histopathologic findings consist of inflammatory cells in the paratenon or peritendinous areolar tissue and loss of tendon collagen, fiber disorientation, vascular ingrowth, but absent or very sparse intratendinous inflammation. The clinical picture is the same as seen in paratenonitis, with frequently palpable tendon nodules, swelling and inflammatory signs.

Tendinosis. Previously named "tendinitis". Intratendinous degeneration due to different etiologic factors characterized histologically by noninflammatory intratendinous collagen degeneration with fiber disorientation and vascular ingrowth. In tendinosis there is no swelling of the tendon sheat, and there can be a palpable tendon nodule.

Tendinitis. Previously named "tendon strain" or "tendon tear". This is a symptomatic degeneration of the tendon with vascular disruption and inflammatory repair response.

Patellar tendinopathy. This term means the lesion associated with pain and tenderness at the lower point of the patella and lesions of the main body of the tendon. It can be used to describe both acute and overuse conditions, but does not assume any knowledge about the underlying pathology.

Jumper's knee. A clinically defined condition with exercise-related pain localized at the quadriceps insertion to the patella or the patellar tendon and its proximal insertion, combined with pain on palpation at the same localization.

Summary

The term "tendinopathy" describes a medical condition associated with a lesion with tendon pain and tenderness. It can be used to describe both acute and overuse conditions. Tendinopathy is assumed to be caused by overload in more or less susceptible individuals. The aim of this thesis was to study certain aspects of this disease in athletes with tendinopathy localized to their patellar tendon, and based on the findings suggest a model that can explain the relationship between a suspected chronic overload injury and the tissue response on macro and cellular level.

The aim of the study presented in Paper I was to estimate the prevalence of jumper's knee in different sports among female and male athletes, in order to correlate the prevalence to the loading characteristics of the extensor mechanism in these sports. The study was designed as a cross-sectional study. We examined approximately 50 Norwegian male and female athletes at the national elite level from different sports. The examination included an interview on individual characteristics (weight, age, height, and training background), a clinical exam and self-recorded VISA score (from 0 (worst) to 100 (best). The overall prevalence of current jumper's knee was 14.2% (87 of 613 athletes), with a significant difference between sports with different performance characteristics (range: 0-45%). In addition, 51 athletes (8%) reported previous symptoms. The prevalence of current tendinopathy was lower among women (5.6±2.2%) compared with men (13.5±3.0%; χ^2 test, p=0.042). The duration of symptoms among athletes with current tendinopathy (n=87) was 32±25 (SD) months with a VISA score of 64±19. The study shows that the prevalence of jumper's knee is high in sports characterized by high demands on speed and power for the leg extensors. The symptoms are often serious, resulting in long-standing impairment of athletic performance.

In Paper II we assessed the ultrasound characteristics of the patellar tendon in two groups of volleyball players, one group without knee symptoms and one group with symptoms of jumper's knee. Of 47 male elite players, 25 were diagnosed to have current and 7 to have had previous symptoms of jumper's knee, as determined by clinical examination. Since some players had bilateral problems, there were 34 knees with current problems and 9 with previous problems. Seven of the 30 knees with a clinical diagnosis of jumper's knee in the patellar tendon had normal ultrasound findings, and ultrasound changes believed to be associated with jumper's knee (tendon thickening, echo signal changes, irregular paratenon appearance) were observed in 12 of 51 knees without symptoms. Specific ultrasound findings such as paratenon changes, hypoechoic zones or pathologic tendon thickness proximally did not correlate significantly with the degree or the

duration of symptoms. This study suggests that the specificity and sensitivity of ultrasonography is low in the evaluation of patients with mild symptoms of jumper's knee.

In Paper III and IV, we examined the biomechanical characteristics of the extensor mechanism in athletes with jumper's knee compared with healthy controls, and described their training background and body characteristics.

In Paper III, patient and control groups (12 players in each) were selected from a population of 141 well trained male Norwegian volleyball players, of which 55 (39%) satisfied the diagnostic criteria for jumper's knee. The testing program consisted of a standing jump (SJ), a counter-movement jump (CMJ), a 15 second rebound jump test (RJ), a standing jump with a 20 kg load ($SJ_{20\ kg}$) and a load corresponding to one-half body weight ($SJ_{1/2\ bw}$). The test result of the patient group was significantly higher than that of the control group for CMJ (15% increase), power during RJ (41%), work done in SJ (12%) and CMJ (22%), and the difference between CMJ and SJ (effect of adding eccentric component). In conclusion, athletes with jumper's knee demonstrated better performance than healthy athletes in jump tests, particularly in ballistic jumps involving eccentric force generation.

In Paper IV, the purpose of the study was to examine the performance of the leg extensors in two groups of high level male volleyball players, one group with jumper's knee (n=24) and a control group (n=23) without knee symptoms. The groups were similar in age, height and playing experience, but the patient group did more specific strength training and had a higher body weight. The testing program consisted of different jump tests with and without added load. Jump height was measured using a contact mat connected to an electronic timer, whereas equipment recording load displacements was used to measure velocity, force and power during jumps with added load. The results showed that the patient group scored significantly higher than the control group on a composite jump index calculated from the individual test results.

In Paper V, we did a case-control study to examine if nerve ingrowth and altered expression of sensory and sympathetic neuromediators may play a major role in the pain pathophysiology of patellar tendinopathy, since the mechanisms behind the occurrence of cronic tendon pain is still largely unknown. Biopsies from the patellar tendon in patients with patellar tendinopathy were compared with biopsies from a control group without any previous or current knee complaints compatible with patellar tendinopathy. The biopsies were stained immunohistochemically for sensory and autonomic nerve markers. With semi-quantitative methodology the biopsies from the two groups were compared. Chronic painful patellar tendons exhibited increased occurrence

of sprouting non-vascular sensory, substance P (SP)-positive nerve fibers and decreased occurrence of vascular sympathetic nerve fibers, positive to tyroxin hydroxylase (TH ; a marker for noradrenaline). Increased occurrence of SP suggests a nociceptive and maybe also a proliferative role in tendinopathy, while the decreased occurrence of TH may reflect a decreased anti-nociceptive role. Further neuro-anatomic studies should be performed for elucidating future specific treatment of tendinopathy.

Paper VI was a case-control study to see if an apoptotic process is part of the pathophysiology in tendinopathy. Apoptosis, also called "programmed cell death", is a specific physiological response to different stimuli with distinct morphological and biochemical changes ending up with cell death. Biopsies from the patellar tendon in patients with patellar tendinopathy were compared with biopsies from a control group without any previous or current knee complaints compatible with patellar tendinopathy. The presence of apoptosis was examined with immunohistochemical methods using a polyclonal antibody recognizing active caspase-3, confirmed by labeling DNA strand breaks (F7-26 antibody) and nuclear morphology. There was a significant higher number of apoptotic cells per unit area in tendinopathic samples compared with controls. Although the tendinopathic samples displayed increased cellularity, the apoptotic index was significantly higher. This study confirms that apoptosis is a feature of tendinosis. This suggests that tenocyte death may either limit the ability of injured tendon to recover from chronic injury, or may be involved in the ongoing repair and remodeling of the chronically injured tendon.

Introduction

Anatomy

Gross anatomy

The patellar tendon extends from the lower patellar pole to the tibial tuberosity and is the extension of the common tendon of insertion of the quadriceps femoris muscle. It is about 3 cm wide in the coronal plane and 4-5 mm deep in the sagittal plane (Khan et al. 1998). The bulk of the tendon is attached to the distal two-thirds of the anterior aspect of the patella with fascicles converging in the frontal plane and parallel in the sagittal plane towards their tibial attachments (Basso et al. 2001). The length of tendon fascicles varies with longer anterior fascicles than the corresponding posterior fascicles, since the anterior bundles are attached more proximal to the patella and more distal to the tibia than the corresponding posterior bundles (Basso et al. 2001).

The tendon is surrounded by a loose areolar connective tissue called the paratenon, which functions as an elastic sleeve and permits free movement of the tendon against the surrounding tissue (Kvist et al. 1985, Hess et al. 1989). Under the paratenon the tendon is surrounded by a fine connective tissue sheath called the epitenon which on its inner side is contiguous with the endotenon. This endotenon invests each tendon fiber and binds individual fibers (Hess et al. 1989, Jozsa et al. 1991). The endotenon network allows the fiber groups to glide on each other and to carry blood vessels, nerves and lymphatics to the deeper portions of the tendon (Hess et al. 1989, Jozsa et al. 1991).

Vascular supply

The arterial supply is from three arterial pedicles on each side of the patellar tendon. Two main arcades anastomose with these pedicles, the retropatellar and the supratubercular resulting in a peritendinous network characterized by a high vascular density next to the poles of the patellar tendon. The retropatellar arch has an average diameter of 1.5 mm and courses horizontally across the fat pad in the posterior surface of the patellar tendon and is placed at the level of junction between the patella and the tendon (Soldado et al. 2002). Only the retropatellar and the supratubercular arches give rise to vessels that pierce the tendon, which means that there are two vascular segments in the arterial supply of the patellar tendon (bipolar pattern). The upper

segment of the patellar tendon is supplied by arterioles that reach the posterior surface from the retropatellar arch and enter the tendon substance from the posterior side. The inferior segment is supplied from arterioles from superficial vessels from collaterals of the supratubercular arch. These intratendinous vessels create anastomoses in the middle third of the patellar tendon (Soldado et al. 2002). In the tendon substance there is an intratendinous vascular network together with nerves and lymphatics localized to the endotenon septas (Elliott 1965, Hess et al. 1989). This intratendinous network consists of longitudinally arranged vessels with one artery followed by two veins. Small arterioles and capillaries originate from these longitudinally arteries and form the microvascular units of the tendon tissue organized to ensure an adequate metabolism in all part of the fiber fascicles (Ippolito 1986).

Cell components

The cellular elements of the patellar tendon consist of 90-95% tenoblasts and tenocytes, the rest are chondrocytes at the insertion sites, nerve and vessel cells (Jozsa and Kannus 1997). The morphologic features of young tenoblasts support the concept that these cells have a high metabolism with high synthesis of the matrix components (Jozsa and Kannus 1997). The tendon cells have the enzyme chains for all of the main pathways of energy metabolism: the Krebs cycle, anaerobic glycolysis and the pentose phosphate shunt (Ippolito 1986, Jozsa et al. 1979).

Innervation

The patellar tendon is innervated mainly by sensory nerves entering the tendon substance via the endotenon septa. Inside the tendon the nerves are relatively few in number and follow the vascular channels, anastomise with each other and finally terminate in the sensory nerve endings (Ippolito 1986, Jozsa et al. 1993). However, the innervation within the patellar tendon and the distribution of the different nerve fiber types within the patellar tendon substance is mostly unknown.

In tendon tissue in general the myelinated A-fibers innervate specialized multicellular end organs with high sensitivity to mechanical stimuli (Bray et al. 2005). The mechanoreceptors found in tendons and ligaments are important in motor control (Proske et al. 1988). The different kinds of free nerve endings, called nociceptors, are activated by mechanical, chemical and thermal stimuli and can be sensitized by repetitive activation (Schepelmann et al. 1992). Stimulation of these nociceptive fibers results in vasodilatation, increased vascular permeability and oedema, which is called “neurogenic inflammation” (Bayliss 1901, Lewis 1937). The autonomic nerve fibers are

mainly localized in networks around blood vessels in the epiligaments and loose connective tissue around the tendons and ligaments (Bray et al. 2005). Both sympathetic and parasympathetic autonomic fibers have been identified in tendons and ligaments (Bray et al. 2005). According to Bray et al. (2005), there are three groups of neurotransmitters of importance in the regulation of tendon and ligament physiology; sensory, opioid and autonomic according to their function and original nerve fiber type. They can act as neurotransmitters, hormones and paracrine factors.

Sensory neuropeptides with nociceptive and pro-inflammatory effect are substance P (SP) and calcitonin gene-related peptide (CGRP) (Ziche et al. 1990). These neurotransmitters are found in pain-transmitting C-fibres (Gibson et al. 1984, Lembeck et al. 1987, Wiesenfeld-Hallin et al. 1984). Substance P is involved in a multitude of physiological processes due to its widespread distribution, centrally and peripherally; among them are angiogenesis and vasodilatation (Konttinen et al. 1990). The autonomic nerve system can influence the sensory C-fibers by sensitizing or desensitizing the pain receptors.

Physiology

Tendons are extremely strong with an ultimate failure-stress range of 56.7±4.4 MPa (Stanish et al. 1985). According to Stanish et al. (1985), tendons may be subject to fatigue with high chronic repetitive loading, despite the fact that the cyclical loads may be well within the tendons ultimate failure-stress range. Physiological loads usually cause less than 4% increase in the length of the tendon and strain above 4% results in damage to one or more of the tendon fibre bundles, while strain in excess of 8-12% results in complete tendon rupture (strain is calculated as change in length per unit length) (Elliott 1965, Jozsa and Kannus 1997, Burstein and Wright 1994). It has been estimated that forces within the patellar tendon may reach 14.5 kN during competitive weight lifting resulting in a total patellar rupture, which corresponds to more than 17.5 times the lifter's body weight (Zernicke et al. 1977). When calculated per cross-sectional area, there is no gender difference in the tensile strength of human tendons (Becker and Krahl 1978). Forces that place highest stress on the tendon occur during eccentric muscle contraction (Fyfe and Stanish 1992, Stanish et al. 1985). The maximal muscle force that can be generated eccentrically is 1.5-2.0 times higher than the maximal isometric force, and several-fold higher than maximal concentric force, especially at high speeds (Herzog 2000). Also, the ground reaction force is different between different tasks, ranging from 2.8 times body weight during distance running to 6 times body weight during jumping in volleyball and 10 times body weight in a long jump take off

(McNitt-Gray 2000). The highest ground reaction forces are seen with ballistic drop jumps, and the resulting forces through the extensor tendons are proportional to the ground reaction force.

In a study by Basso et al. (2002), they found that under quadriceps loading there was significantly higher strain in the posterior fascicles compared with the anterior fascicles between 60 and 90 degrees of knee flexion. The material properties in the anterior and posterior fascicles were similar, except that the failure strain was significantly higher posterior. For a same amount of elongation, the shorter posterior fascicles strain more than the longer anterior fascicles. This could mean that the posterior fascicles are adapted to sustain significantly greater tensile strain before failing (Basso et al. 2002). However, in a recent study by Almekinders et al. (2002), they found that the strain increased on the anterior side but decreased on the posterior side in the central, proximal location of the tendon in dynamic measurements in the range from 0 to 60 degrees of flexion. The cross-sectional area of the tendon increases from proximal to distal (el-Khoury et al. 1992). Since shear stress is directly correlated to the cross-sectional area, the shear stress can therefore be assumed to be higher in the proximal part of the tendon compared with the distal part.

Pathology

Histopathology

The histopathological findings in biopsies from the patellar tendon in patients with tendinopathy are very consistent. Under light microscopy the biopsies are characterized by degeneration and fibrotic scarring in the tendon itself, as well as in the bone-tendinous junction (Ferretti et al. 1985, Fritschy and de Gautard 1988, Kälebo et al. 1991, Myllymäki et al. 1990, Orava et al. 1986, Raatikainen et al. 1994, Roels et al. 1978). The normal parallel collagen bundles are disorganized and replaced by degenerative tissue with increased ground substance, consisting of proteoglycans and glycosaminoglycans (Khan et al. 1996). The tenocytes lose their spindle shape and nuclei appear more rounded (Clancy 1990). There are an increased number of fibroblasts compared with normal tendons (Ferretti et al. 1983, Colosimo and Bassett 1990, Fritschy and deGautard 1993, Roels et al. 1978, Martens et al. 1982). There is also neovascularization with capillary proliferation and prominent angiogenesis (Roels et al. 1978, Colosimo and Bassett 1990, Khan et al. 1998). There are clefts in the collagen bundles, which have been assumed to represent microscopic tears in the tendon substance (Roels et al. 1978, Davies et al. 1991, Kujala et al. 1989, Raatikainen et al. 1994). In a recent presentation, Maffulli et al. (2005) reported similar

histopathological findings in tendinopathic Achilles and patellar tendons. They stated that "a common, as yet unindentified, etiopathological mechanism may have acted on both these tendon populations." This means that there may be a common pathophysiological pathway that may explain the very uniform histopathological findings in tendinopathic tissue biopsies.

One of the most striking findings is the absence of inflammatory cells. As stated by Khan et al. (1998), there are two papers coauthored by specialist pathologists who report a total absence of inflammatory cells in tissue from patients with jumper's knee, even at the periphery of abnormal tissue and in patients who had symptoms for only four months (Yu et al. 1995, Khan et al. 1996). In a study by Alfredsson et al. (2003), they used cDNA arrays and real-time quantitative polymerase chain reaction technique to study tendinosis and control tissue samples and found that several cytokines and cytokine receptors were not upregulated, indicating the absence of an inflammatory process in chronic painful Achilles tendinosis.

Cell pathology

However, one consistent finding in biopsies from tendinotic tissue is hypercellularity. In the absence of inflammatory cells, the hypercellularity must be explained by the presence of other cell types. These cells are not fully characterized.

Recently, it has been suggested that the initial pathology in tendinopathy is to the tenocyte, not the collagen fibres (Khan et al. 2000b, Yuan et al. 2003, Cook et al. 2004). Necrosis and apoptosis are the two major types of cellular death (Ameisen 1996, Lavin and Watters 1993, Sen 1992). Necrosis is characterized by rupture of the cell membrane and very often an inflammatory response and a pathological tissue reaction involving groups of adjoining cells (Ameisen 1996). Apoptosis, also called "programmed cell death," is a specific physiological response to different stimuli with distinct morphological and biochemical changes ending up with cell death, very often without a concomitant inflammatory response (Lavin and Watters 1993, Sen 1992). The apoptotic process is stimulated and inhibited by a number of influencing factors, such as hormones, cytokines and growth factors (Kiess and Gallaher 1998). At the cellular level the tendon cells are also influenced by mechanical factors, such as repetitive loading and stretching (Skutek et al. 2003, Barkhausen et al. 2003, Arnoczky et al. 2002). In a study by Yuan et al. (2002), they found excessive apoptosis at the edge of torn rotator cuff tendons compared with controls. However, in this study the mean age of the patients was more than 60 years and they had a rupture of the rotator cuff. Tendon rupture may result from a different pathological process compared to tendinosis. This means that the findings by Yuan et al. (2002) cannot necessarily

explain the pathology found in tendinopathic tissue biopsies. In a study by Scott et al. (2005) they showed that apoptosis could occur in response to short term, high strain mechanical loading in a rat tibialis anterior model. This means that there is evidence for a connection between mechanical factors and apoptosis both at the cellular level and at the isolated tendon level. These findings suggest that apoptosis may be a factor in tendon overload injuries. However, it is still unknown whether there is a connection between mechanical factors and apoptosis in vivo in humans. This problem was explored in Paper VI.

Vascular pathology

Another consistent histopathological finding in tendinotic tissue biopsies is neovascularization with capillary proliferation and prominent angiogenesis (Roels et al. 1978, Colosimo and Bassett 1990, Khan et al. 1998). This neovascularization may be a part of the remodeling process, but is assumed to weaken the mechanical stability by proteolysis of the extra-cellular matrix by the invading endothelial cells (Petersen et al. 2004b). Angiogenesis is controlled by many stimulatory and inhibitory proteins acting on invading endothelial and smooth muscle cells (Ferrara 1999). One of the most important angiogenetic factors is vascular endothelial cell growth factor (VEGF) (Senger et al. 1983). High VEGF concentrations have been demonstrated in degenerative tendon tissue compared with healthy Achilles tendons (Pufe et al. 2001, Petersen et al. 2004a). In response to VEGF stimulation vascular and smooth muscle cells produce matrix metalloproteinases (MMPs) (Wang and Keiser 1998, Sato et al. 2000). The protease inhibitor tissue inhibitor of metalloproteinase-3 (TIMP-3) blocks VEGF from binding to its receptor VEGFR-2, thereby reducing the effect of VEGF (Qi et al. 2003). This means that there are interactions between VEGF and MMPs and TIMPs resulting in weakened material properties in the tendon in degenerative tendon disease (Pufe et al. 2005). Another regulatory pathway of VEGF production is by the transcription factor hypoxia inducible factor-1 (HIF-1). VEGR is upregulated by HIF-1, and HIF-1 is upregulated by hypoxia (Maxvell et al. 2001, Ferrara 1999). In a study by Petersen et al. (2004b), they found that mechanical stress induced HIF-1 and VEGF in isolated tendon cells. This means that both hypoxia and mechanical factors influence the expression of VEGF. The role of VEGF and HIF-1 in the angiogenetic process seen in biopsies from patients with patellar tendinopathy is not known.

Healing processes

The reparative processes in tendinosis are also poorly understood. Whether tendinosis is a primary degenerative condition, or if there are simultaneous degenerative and reparative processes within the tendon substance is unknown. Many growth factors and matrix molecules with different biological effects can be found in the tendon substance with different temporal expression (Dahlgren et al. 2005). Both insulin-like growth factor-1 (IGF-1) and transforming growth factor ß1 (TGF-ß1) are produced by tenoblasts, and in vitro these two growth factors increase cell proliferation and the synthesis of collagen and proteoglycans (Abrahamsson et al. 1991, Letson and Dahners 1994, Tsuzaki et al. 1994). Whether these growth factors are up-regulated in tendinotic tissue is not known. If there is an increased expression of IGF-1, this may, at least in part, explain the hypercellularity found in biopsies from tendinotic tissue. An increased expression of IGF-1 would also indicate an ongoing reparative process within the tendon tissue.

Pain mechanisms

In the absence of inflammatory cells, the substrate for pain production is confusing. In biopsies from degenerated facet joints and degenerated intervertebral discs it has been shown that there is in-growth of nociceptive nerve fibers (Freemont et al. 1997, Coppes et al. 1997, Konttinen et al. 1990). It is not known whether this is part of the pain mechanism in tendinopathy. In a study by Bjur et al. (2005), they examined the innervation pattern of the normal and tendinotic Achilles tendon and found SP and CGRP in the paratendinous loose connective tissue and to some extent in the tendon tissue proper intimately associated with small blood vessels. However, as described earlier, the innervation and distribution of the different nerve fiber types within the patellar tendon substance is unknown. The pain mechanisms in patellar tendinopathy are also mostly unknown. These issues were the focus of Paper V.

Diagnosis of patellar tendinopathy

The diagnosis of jumper's knee is based on a history of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with athletic activity and distinct palpation tenderness corresponding to the painful area (Blazina et al. 1973). The diagnosis of patellar tendinopathy requires that, in addition to a typical history and clinical signs, there are structural changes in the tendon, as demonstrated by MR, ultrasound or tendon biopsies. Nevertheless, in the clinical setting the diagnosis is often based on a typical history and clinical findings alone.

In fact, when the current research projects were started, the relationship between imaging findings and symptoms had not been clarified. Previously the diagnostic precision by use of ultrasound was assumed to be high, since several studies had shown a near-perfect correlation between preoperative ultrasound changes and surgical findings (Raatikainen et al. 1994, Orava et al. 1986, Kälebo et al. 1991, King et al. 1990, Karlsson et al. 1992). However, as these studies were carried out in a selected patient group (i.e. almost all of them had disabling symptoms who did not respond to non-operative treatment), the results should be interpreted carefully when applied to other patient populations.

The only previous study comparing the clinical and ultrasound-based diagnosis of jumper's knee was done by Myllymäki et al. (1990). Of 62 knees with characteristic symptoms of jumper's knee, they reported no hypoechoic changes in 31 (50%). However, to our knowledge, there is no available information on the histopathological changes in patients with Roels' grade I, II or IIIa disease. In spite of lack of this information, attempts had been made to correlate ultrasound changes and anatomical findings to the clinical staging of the disease (Fritschy and DeGautard 1988, Jerosch et al. 1990). Jerosch and Schröder (1990) suggested that a relationship exists between the severity of the pathological changes and certain ultrasound characteristics. However, their study did not include corresponding histopathological examinations, which means that their conclusions were based on assumptions. In Paper II, we have examined the ultrasound characteristics of the patellar tendon among high-level volleyball players with and without jumper's knee.

To assess the severity of the disease Roels' clinical grading system (Roels et al. 1978) has been used. It is assumed that this grading system reflects the clinical seriousness of the disease, but the system is based more on clinical experience than research. In describing patients with jumper's knee, we proposed a modification to Roels' clinical grading system. There are several patients who are able to play matches and practice despite having pain throughout the activity, but for whom there is no available classification category according to Roels et al. (1978). We therefore suggested splitting grade III into grade IIIa for patients with pain during activity, but who are still able to train and play matches, and grade IIIb for those with disabling pain (Table 1). This modification would enable a more precise patient classification in future epidemiological and clinical studies.

Table 1. Classification of jumper's knee according to symptoms as outlined by Roels et al. (1978) as modified by us.

	Roels et al. (1978)	Our classification
Grade I	*Pain* at the infrapatellar or suprapatellar region *after practice* or after an event	Same
Grade II	*Pain at the beginning of the activity, disappearing after warm-up and reappearing after completion of activity*	Same
Grade III	*Pain remains during and after activity* and the patient is *unable to participate* in sports	IIIa: *Pain during and after activity, but the patient is able to participate* in sports at the same level IIIb: Pain during and after activity and the *patient is unable to participate* in sports at the same level
Grade IV	*Complete rupture of the tendon*	Same

In order to assess the severity of the condition, athletes diagnosed with patellar tendinopathy can self-record their VISA score (Visentini et al. 1998). This is a validated pain and function score with a best score of 100 (no symptoms) and lowest score of 0 (maximum symptoms), which has been developed specifically for this purpose and has been shown to be a valid measure of symptoms (Robinson et al. 2001).

Epidemiology of jumper's knee

The prevalence of jumper's knee across different sports is mostly unknown. However, early studies from volleyball have shown that among male players at the elite level the prevalence is 40-50 % (Ferretti et al.1983, Ferretti et al. 1990). Publications from studies on the outcome after surgery suggest that the prevalence may be high in sports with high demands on speed and power, such as volleyball, soccer and athletics (Karlsson et al. 1991, Raatikainen et al.1994, Martens et al. 1982). Raatikainen et al. (1994) from Finland described 182 patients undergoing surgery for jumper's knee and found that 46% were from athletics, 37% from volleyball, 5% from soccer and the rest from other sports. On the other hand, Martens et al. (1982) from Belgium found that only 8% of his 90 surgically treated patients were from athletics, while 34% were volleyball players and 32% soccer players. Furthermore, Karlsson et al. (1992) from Sweden reported that of 81 patients they treated for jumper's knee, only 9% were volleyball players, while 37% were from athletics and 27% from soccer. In all of the three studies described, basketball

accounted for less than 10% of patients. As illustrated by the conflicting results from these (Karlsson et al. 1992, Raatikainen et al. 1994, Martens et al. 1982) and other studies (for a complete review of surgical studies, see Coleman et al. 2000), is not possible to estimate prevalence from case series, since the population at risk is unknown. The differences observed in the proportion of patients from different sports may simply reflect how popular these sports are in the different countries. To our knowledge, there are no previous reports on the prevalence of jumper's knee across different sports, nor is the severity and duration of symptoms well described across sports. This issue was therefore examined in Paper I.

Intrinsic risk factors for patellar tendinopathy

In general, risk factors for sports injuries are traditionally divided into internal, personal, risk factors and external, environmental, risk factors which can act either alone or in combination (Lorentzon 1988, Stanish 1984, van Mechelen et al. 1992). In tendon overuse injuries, an interaction between these two categories is common (Harvey 1983, Williams 1986).

According to Hess et al. (1989), almost any orthopaedic disorder that causes a variation from normal anatomic position and resulting vector forces on a tendon may cause an overuse syndrome. The most common intrinsic factors suggested in tendon overuse injuries are said to be alignment abnormalities, leg length discrepancy, muscle weakness and imbalance, decreased flexibility, joint laxity, gender, age, overweight and predisposing diseases (Hess et al. 1989, Micheli 1983, Renström 1988, Heiser et al. 1984, Kannus et al. 1987, Drinkwater 1988). Most of these references are review articles and none of them specifically address patellar tendinopathy. As stated by Lorentzon (1988); in general, it should be stressed that this area is highly conjectural and that many plausible hypotheses lack substantial evidence. It is claimed that in elite athletes a leg length discrepancy of more than 5 to 6 mm may cause symptoms (Michaeli 1983, Renström 1988). However, the clinical significance of leg length discrepancy is uncertain and further investigations in athletes providing substantiating data are needed before any firm conclusions can be drawn (Lorentzon 1988). Muscle imbalance means that there is an asymmetry between the agonist and the antagonist muscles in one extremity, asymmetry between the extremities, or a difference with an anticipated normal value (Grace 1985). The actual magnitude of what constitutes balance and imbalance has never been accurately defined and may actually be dependent on anatomic region involved, type of sport, age, size and gender (Grace 1985). There is some evidence that certain conditioning programs can reduce the injury rates related to muscle weakness or imbalance (Heiser et al. 1984), but other studies could not find any relationship

between muscle weakness or imbalance and injury (Grace 1985). As far as we know, there are no studies investigating the connection between patellar tendinopathy and muscle imbalance. Moreover, there are no studies to provide conclusive evidence on whether reduced flexibility is the cause or the consequence of tendon injuries (Jozsa and Kannus 1997).

Gender

According to Kannus et al. (1987) and Drinkwater (1988), there is a higher incidence of tendon overuse injuries among females compared with men. Women have less muscle mass per unit body weight than equally trained men, and their overall muscle strength averages about two-thirds that of men (Drinkwater 1988). Jozsa and Kannus (1997) suggest on a theoretical basis that these factors together with female risk factors in body anatomy and biomechanics (i.e., wider hips and more mobile joints) may predispose women to overuse injuries. Ferretti (1986) also presented the results from a sample of 26 volleyball players selected from 93 players diagnosed with jumper's knee in a random cohort of 407 volleyball players participating in the Italian Volleyball Championship. The selection criteria were not described and there was no control group. They found no difference in the prevalence of jumper's knee between males and females. In other words, there is limited epidemiological evidence to substantiate the claim for a gender bias in overuse tendon injury risk. This issue was studied in Paper I.

Antropometric data, strength and flexibility

Data on intrinsic factors for patellar tendinopathy are conflicting, and mostly related to static biomechanical characteristics (Ferretti et al. 1984, Kujala et al. 1986, Kujala et al. 1987). In a study by Hunter and Pole (1987), they suggest that "patellar tendinitis" can be caused by tight hamstring and quadriceps muscles and treated by flexibility training. However, this study does not give any information on flexibility measurements or specific outcome measures to support their suggestions.

In a study by Witvrouw et al. (2001), they followed 138 students without any knee complaints at inclusion for two years. At inclusion all students were evaluated for leg alignment characteristics, muscular tightness, and muscular strength. The leg length alignment characteristics were obtained by clinically measuring the leg length discrepancy, Q-angle and the medial tibial intercondylar distance. Isokinetic strength of the quadriceps and hamstring muscles were evaluated on a dynamometer. The tightness of the hamstrings and quadriceps femoris muscles were measured goniometrically. Nineteen of these 138 students developed "patellar tendonitis" based on clinical

and ultrasonographic examinations. Univariate and stepwise discriminant function analysis were performed on different measurements, and the only significant factor was muscular flexibility, with the patellar tendonitis patients being less flexible in the quadriceps and hamstring muscles ($p< 0.05$). To explore this issue, stretching and warm-up habits were compared between athletes with jumper's knee and controls in Paper III and IV.

In a study by Ferretti et al. (1984) among 407 male volleyball players they found a small peak in incidence between 20 and 25 years and an incidence peak at the third year of play, but concluded that age and years of play were not significant factors in producing jumper's knee. Age and years of play as intrinsic predisposing factors are examined in Papers I, III and IV.

In another study by Ferretti et al. (1983), primarily on histological findings in biopsies from athletes with jumper's knee, they also report that out of 18 knees treated surgically, two patients had patella alta and eight had a vastus medialis obliquus dysplasia. However, none of these patients were characterized further in the text, and the diagnostic criteria used were not described.

Ferretti (1986) also presented the results from a sample of 26 volleyball players selected from 93 players diagnosed with jumper's knee in a random cohort of 407 volleyball players participating in the Italian Volleyball Championship. The selection criteria were not described and there was no control group. Evaluation of the knee alignment, alignment of the extensor mechanism, position of the patella, characteristics of the tibial tuberosity, rotation of the femur, rotation of the tibia, degree of constitutional instability, characteristics of the foot or morphotype, did not give conclusive results with regard to predisposing intrinsic factors.

Leg length and patellar position

In the same study by Ferretti (1986) they assessed the position of the patella both clinically and radiographically using the method of Insall and Salvati (1971), and concluded that the patella was "slightly high" in four out of 26 athletes diagnosed with jumper's knee. However, they did not specify whether this finding was based on clinical or radiographic methods, or both.

In contrast, in a series of papers by Kujala et al. (1986, 1987, 1989) they found more leg length inequality and patella alta in patients with jumper's knee compared to controls. They compared 20 athletes diagnosed with jumper's knee with a control group of 20 athletes with normal knees and found a significantly higher mean value for lower leg length inequality in the athletes with jumper's knee compared with the control group (7.3 mm $\pm$ 4.2 mm vs. 3.0 mm $\pm$ 2.3 mm,

$p<0.001$) (Kujala et al. 1986). In the same study, they measured patellar height using two different methods. The Insall-Salvati method relates the length of the patellar tendon to the length of the patella (Insall and Salvati 1971), while the method described by Blackburne and Peel (1977) measures the ratio between the shortest distance from the distal end of the articular surface of the patella and the tibial plateau to the length of the articular surface of the patella. Using the Insall-Salvati method they found a significantly higher position of the patella in the patient group, but no significant difference with the Blackburne-Peel method. It should be noted that in this study 13 of the 20 athletes in the patient group were volleyball players, while only four out of 20 in the control group were volleyball players, which reduces the validity of this study. In a later study they used radiographic methods and found that the leg length inequality among athletes diagnosed with jumper's knee to be 5.8 ± 4.5 mm compared to 3.0 ± mm in a control group (Kujala et al. 1987). In this cohort of 57 athletes with jumper's knee there were 37 volleyball players, three basketball players, four long distance runners and five orienteerers. Ten athletes were not characterized with regard to type of activity. In the athletes with jumper's knee the injury was located on the side with the longer leg in 17 of 27 (63%) of cases. The same group of athletes had the injury located to the takeoff leg in 30 cases and on the other side in 18 cases. Those who could determine their take-off leg when jumping and whose lower leg inequality was at least 5 mm, the takeoff leg was the longer in 15 cases and the shorter leg in seven cases. However, they provided no information on the connection between types of sport or takeoff technique, nor whether these were statistical significantly differences.

In a final study by the same group (Kujala et al. 1989), they studied the extensor mechanism in 32 male competitive volleyball players and a control group of 49 young males. In this study they used both the Insall-Salvati index and the Blackburne-Peel index to evaluate the height of the patella, and concluded that there was a slight, but significant ($p<0.05$) tendency to patella alta according to the Blackbourne-Peel index, but no difference based on the Insall-Salvati index. In this study the control group was selected from volunteers at the beginning of their military service, making selection bias possible. The internal validity in this study is substantially reduced since the control group was not representative with regard to other known factors that could render them susceptible to jumper's knee. As a conclusion, based on this series of studies, there are conflicting results on the relationship between patella alta and jumper's knee. However, a methodological limitation with these studies is the fact that the patient group and the control group were from different sports. In this thesis, the position of the patella was examined in Paper II, using the Insall-Salvati index, comparing athletes with patellar tendinopathy with controls from the same sport and with identical training background.

In all of the previous studies described, the main study focus was on static biomechanical parameters. In Paper III and IV we have examined dynamic characteristics of the extensor mechanism, which may have a stronger effect as predisposing internal factors since they reflect the loading pattern during training and competition.

Patellar impingement

Johnson et al. (1996) postulated that impingement of the inferior patellar pole against the patellar tendon during knee flexion is responsible for "patellar tendonitis". They studied 24 patients diagnosed with patellar tendonitis and concluded that there was impingement of the inferior patellar pole against the patellar tendon by examining the involved knee in a position of 60º of flexion. In this study they were able to demonstrate kinking between the patella and the patellar tendon, but the reproducibility of their positioning protocol was questioned by the authors themselves. In another study by Schmid et al. (2002), they examined 19 knees diagnosed with patellar tendinopathy with positive MRI findings and a typical history and clinical findings. The control group was 32 asymptomatic knees. They obtained dynamic sagittal images from full extension to 100º of flexion with and without activation of the quadriceps muscle and measured the tendon-patella angle, anteroposterior diameter of the tendon, signal-to-noise ratio, the shape of the inferior patellar pole and the location of the patellar tendon insertion. They found no significant difference between the groups of the tendon-patella angle at any angle, with or without quadriceps muscle activation. The insertion site of the patellar tendon differed significantly with a more posterior insertion being more common in symptomatic knees, but not the shape of the inferior pole of the patella. The volume and the signal -to-noise ratio of zones of increased intratendinous signal, as well as the anteroposterior diameter of the proximal patellar tendon were increased in symptomatic knees. The conclusion of this study was that the data could not support the theory that patellar tendinopathy is caused by patellar impingement, because no difference was detected between symptomatic and asymptomatic knees. In this study, the MR examination protocol differed from the protocol used by Johnson et al. (1996), since the images were obtained through a larger range of motion, with a larger number of measurements at different angles of knee flexion with and without activation of the quadriceps muscle. This means that the study protocol in the study by Schmid et al. (2002) is more valid with regard to the problem they investigated in these studies.

Extrinsic risk factors for patellar tendinopathy

Extrinsic predisposing factors act externally on the human body (Nigg 1988). The most common extrinsic factors are thought to be training errors, excessive loads on the body, poor environmental conditions and poor equipment (Nigg 1988, James et al. 1978, Renström and Johnsen 1985, Smart et al. 1980, Ferretti et al. 1984). Training errors are assumed to contribute to 60 to 80% of tendon and other overuse injuries (James et al. 1978, Renström and Johnsen 1985, Smart et al. 1980), and the main problems are thought to be too high intensity and too fast progression. And as stated by Leadbetter (1992), a sport injury is likely to occur when the athlete changes the mode or use of the involved part of the body. This is called "the principle of transition". However, most papers on this subject are theoretical assumptions and mostly related to running injuries.

Training load

In one of the previously described studies by Ferretti et al. (1984), they examined 407 volleyball players from different playing levels and found the overall prevalence of previous or current symptoms of jumper's knee to be 23% (74 men and 19 women). Of those athletes playing five times a week or more, the prevalence was 41%. There was a near linear relationship between the prevalence of jumper's knee and the number of weekly training and playing sessions. However, they did not find any significant correlation between career duration and the prevalence of jumper's knee.

Floor hardness

The ground reaction forces during landing and take-off can be quite different on different surfaces. The impact force or the force at first contact is much higher for running on asphalt compared with running on grass or sand (Nigg 1988). The ground reaction force is at the same magnitude for those different surfaces, and it is therefore speculated that these high-impact forces are one of the causes of overuse injuries (Nigg 1988). Ferretti et al. (1984) found that 60.7% of the players with jumper's knee played on a cemented or linoleum floor, while only 4.7% of those diagnosed with jumper's knee played on a parquet floor, suggesting a positive correlation between the hardness of the floor and the prevalence of jumper's knee among volleyball players. In line with this, it has recently been shown that the prevalence of jumper's knee among elite beach volleyball players playing on sand is only 9%, considerably lower than for indoor volleyball players (Bahr and Reeser 2003).

As stated previously, the ground reaction force is 6 bw during jumping in volleyball and 10 bw in a long jump take-off (McNitt-Gray 2000). The highest ground reaction forces are seen with ballistic drop jumps, and the resulting forces through the extensor tendons are proportional to the ground reaction force. This may explain the correlation between the number of weekly training sessions and the prevalence of jumper's knee as shown by Ferretti et al. (1984). Other predisposing external factors for jumper's knee than hardness of the floor and number of weekly training sessions have not been examined.

Methodological considerations

From a methodological point of view, predisposing factors for overuse injuries are traditionally divided into external and internal factors. However, this model is unidimensional and does not take into account the dynamic interactions between different risk factors. As stated by Bahr et al. (2003), there is also a need to identify the mechanisms by which the injuries occur, and to consider the temporal dimension in a dynamic multicausal model. One such model is described by Meeuwisse (1994).

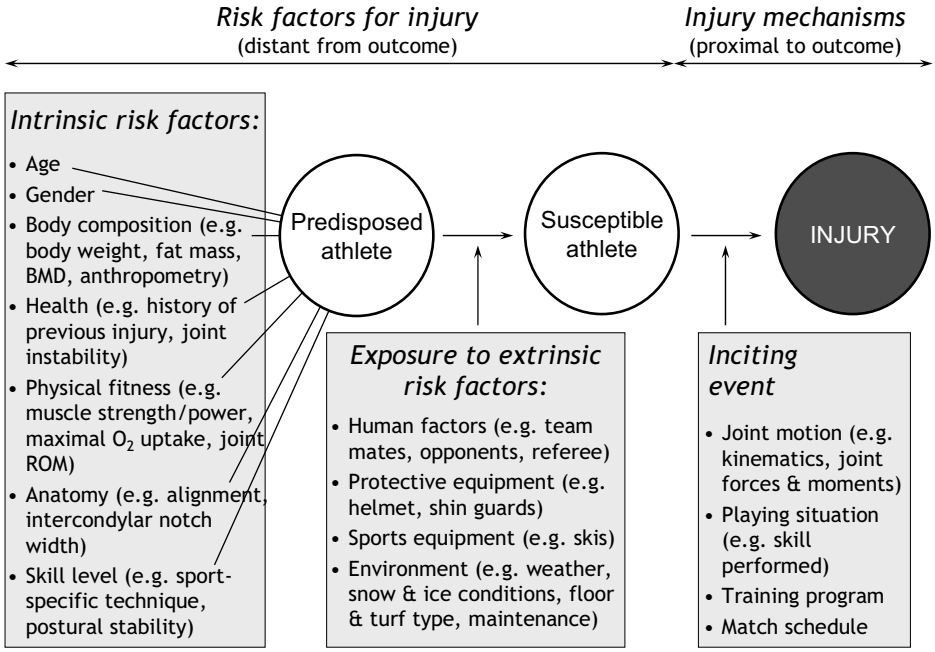


Figure 1. A dynamic, multifactorial model of sports injury etiology as presented by Meeuwisse (1994) and modified by Bahr and Holme (2003) and Bahr and Krosshaug (2005).

This model was mainly developed to describe the etiology of acute injuries. Meeuwisse (1994) states that it is the presence of both intrinsic and extrinsic risk factors that renders the athlete susceptible to injury, but that these factors are not necessarily sufficient to produce injury. In his model the risk factors define a specific predisposition to injury, but there has to be a final inciting event to result in an injury. A specific final event can usually not be identified in the case of overuse injuries, such as patellar tendinopathy. The onset of symptoms is typically gradual and the pathological processes within the tissue may even start a long time before symptoms occur. Therefore, in overuse injuries it may be necessary to study more distant etiological factors to establish a basic understanding of the early pathological processes and in that way be able to establish prophylactic and treatment procedures. Thus, the conceptual model by Meeuwisse (1994) cannot be applied directly to explain the etiology of overuse injuries, but has to be modified to characterize the etiologic factors for overuse injuries. This is highlighted by Bahr and Krosshaug (2005), who emphasize the need to use a comprehensive model, which accounts for the events leading to the injury situation as well as to include a description of whole body and joint biomechanics at the time of injury. In their model different intrinsic and extrinsic factors affect load and load tolerance, and can be used to study the interaction between the different factors causing injury (Bahr and Krosshaug 2005). They state that the key point to consider with regard to biomechanical factors is that they must explain how the event either resulted in a

mechanical load in excess of that tolerated under normal circumstances or reduced the tolerance levels to a point at which a normal mechanical load cannot be tolerated (Bahr and Krosshaug 2005, Mcintosh 2005).

However, the connection between a biomechanical load and the biologic response at the cellular level within the tendon substance is poorly understood. This connection is suggested by Khan et al. (1998), who have described a theoretical model on how tendon injury may precipitate a vicious cycle ("tendinosis cycle") of further injury, modified from Leadbetter (1992). In this model he suggests that an increased demand on the tendon causes microdamage with inadequate repair resulting in inadequate collagen and matrix production. In turn, this results in tenocyte death from excessive strain with further reduction in collagen and matrix production and a predisposition to further injury (Khan et al. 1998). In this model the tendon loading conditions can be regarded as an extrinsic inciting event, and Khan et al. (1998) suggests that there is a correlation between tendon overload and a pathologic response on the cellular level with tenocyte death. Interestingly, he even suggests that susceptible tenocytes may die as a result of excessive strain. In other words, he hypothesizes that there is a connection between a defined biomechanical loading of tendons (strain) and a physiological well-defined response, namely cellular death.

However, all these models are theoretical, and there is an obvious need for specific studies to establish evidence-based models. The overall aim of the present thesis was to examine potential risk factors for patellar tendinopathy and to examine some of the possible cellular responses to these risk factors.

Study aims

Based on the literature outline provided above, the aims of this thesis were as follows:

1. To estimate the prevalence of jumper's knee in different sports, in order to correlate the prevalence to the loading characteristics of the extensor mechanism in these sports and to assess the duration and severity of the symptoms (Paper I).

2. To investigate if there is a gender difference in the prevalence of jumper's knee (Paper I).

3. To compare anthropometric characteristics as risk factors for jumper's knee between athletes with jumper's knee with non-symptomatic controls (Paper I, III, IV).

4. To compare sport history and training background as risk factors between athletes with jumper's knee and non-symptomatic controls (Paper I, III, IV).

5. To characterize differences in the performance ability of the leg extensors in athletes with jumper's knee compared with a control group without knee symptoms (Paper III, IV).

6. To characterize the ultrasound findings of the patellar tendon in athletes diagnosed with jumper's knee compared with non-symptomatic athletes (Paper II).

7. To study some potential pain mechanisms in patellar tendinopathy (Paper V).

8. To study the histopathological findings in biopsies from patients with jumper's knee compared with a control group without knee symptoms (Paper VI).

Methods

Interview and clinical examination

Study populations and interviews

Paper I. This study was designed as a cross-sectional study among Norwegian athletes at the national elite level from different sports. Male athletes from eight different sports were examined; athletics (high jump, 100 and 200 m sprint), basketball, ice hockey, orienteering, road cycling, soccer, team handball, volleyball and wrestling. In addition, female athletes from two of the same sports were examined; team handball and soccer. We wanted to examine approximately 50 athletes in each sport, to provide a precision of 2-7% (proportion standard error) for the prevalence estimate in each group. In the team sports (basketball, ice hockey, team handball and soccer), elite division teams from the largest cities were invited to take part in the investigation, and all invited teams agreed to take part. The teams were examined towards the end of their competitive season. In the individual sports (athletics, orienteering, road cycling, wrestling), we asked athletes participating in the national championships, which were organized during the peak competition season, to take part in the study. All athletes who were present when we visited their team and all athletes we approached in the individual sports agreed to take part in the study.

Paper II and IV. This cohort study was carried out during an international volleyball tournament in Oslo, Norway in May 1994. The tournament was played 2 months after the end of the regular league season with teams competing in classes according to their level of play. The six Norwegian teams participating in the men's elite division in the tournament were invited to take part in the study. These were amateur teams that otherwise competed in the top division of the Norwegian Volleyball Federation (NVBF) leagues. The teams consisted of 53 players and of these, 47 (89%) consented to participate in an interview, a clinical examination, and an ultrasound examination of both knees. Each player went through an interview, and both knees were examined. They were asked about present and former knee injuries and complaints, specifically about symptoms of jumper's knee. Their symptoms were classified according to criteria by Roels et al. (1978), and Blazina et al. (1973). The 47 players who consented to take part were tested with a series of standardized jump and power tests described below. Their patellar tendons were also examined ultrasonographically.

Paper III. In this case-control study the patient and control groups were recruited from division I and II teams in the Norwegian Volleyball Federation (NVBF) leagues, which consisted of 16 men's teams with a total of 164 licensed players. Of these, 141 players participated in two tournaments in September 1989 just prior to the start of the indoor season and these players were interviewed during the tournaments. The athletes in this study were asked about warmup and stretching habits, type of floor in their normal training gym, type of shoe normally worn during volleyball training, as well as data on present and former knee injuries to ensure an identical matching as possible. All players with current knee complaints or a history of previous injury consented to go through a clinical interview and a standard knee examination. Players with current symptoms of jumper's knee were encouraged to report at the testing station for jump testing if they satisfied the following criteria: 1) Symptoms from the patellar tendon only; and 2) No history of intraarticular pathology (positive patella grinding test, positive meniscal tests, instability, locking, 'giving way' or joint effusion), rheumatic disease, previous fractures in the knee region, previous knee surgery or previous corticosteroid injections in or around the patellar tendon. A total of 12 players of those who reported for jump testing satisfied the criteria for inclusion in the patient group and successfully completed the standardized jump testing program. Also, a matched control group consisting of 12 players without knee pain consented to undergo an identical testing program. The control group consisted of players with no history of knee pain and a normal knee examination. The players in the control group were actively recruited to undergo the jump testing programs among team members of the injured players and the players were individually matched with respect to age, function (middle blocker, outside hitter, setter), playing experience and training level.

Paper V and VI. The patient group was selected among athletes from different sports who had failed conservative treatment for patellar tendinopathy. The diagnosis was based on a typical history and clinical findings combined with positive MRI findings compatible with tendinosis to ensure that the biopsies were taken from an area which was assumed to contain pathological tissue. The duration of symptoms had to be more than 3 months.

The control group was selected from patients with tibia fractures from low-energy trauma treated with marrow-nailing. These patients could not have current or previous knee complaints compatible with previous or current patellar tendinopathy. All individuals in both groups had to be more than 18 years old to ensure closed epiphyses. Exclusion criteria in both groups were previous surgical treatment in or around the same knee, previous corticosteroid injections in or

around the same knee, previous serious traumatic events affecting the same knee, all types of rheumatic disease and degenerative knee disorders.

Each patient went through a standardized interview, and the information requested from each athlete included age, height, weight and number of years participating in organized athletic training. Patients were asked to report the number of training hours per week during the competition season (sport specific training, weight training, jump training and other types of training). In order to assess the severity of the condition, the athletes diagnosed with current patellar tendinopathy also self-recorded their VISA score (Visentini et al. 1998).

Diagnostics

Standard form

In all studies information requested from the athletes included age, height, weight, number of years participating in organized training, years of participation at the elite level, total number of training hours per week, number of hours sports specific training per week, weight training and jump training (plyometric training) done each week.

Each athlete went through a standard knee examination and clinical interview on present and former knee injuries and complaints. The following diagnostic criteria for jumper's knee were used: History of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with volleyball play and distinct palpation tenderness corresponding to the painful area (Blazina et al. 1973). Previous jumper's knee was diagnosed based on history alone.

In order to assess the severity of the condition, the athletes diagnosed with current jumper's knee in study III and IV were classified according to Roels et al. (1978) as modified by us (see Table 1, p. 18)

In order to assess the severity of the condition in paper IV, V and VI, the athletes diagnosed with current patellar tendinopathy self-recorded their VISA score (Visentini et al. 1998). This is a validated pain and function score with a best score of 100 (no symptoms) and lowest score of 0 (maximum symptoms), which has been developed specifically for this purpose and has been shown to be a valid measure of symptoms (Robinson et al. 2001).

Biomechanical testing

Paper III. In the first biomechanical study, the testing program was carried out using the Ergojump® equipment (KB Ergotest, Mikkeli, Finland), which consists of a contact mat connected to an electronic timer/computer (Bosco and Komi 1979, Bosco et al. 1983, Komi and Bosco 1978, Sale 1990). The equipment measures the flight time of each jump, and the jump height (in cm) is calculated from this. In addition, power (W) is calculated from flight and contact times during rebound jumping (Bosco et al. 1983). The jumps performed were standing jump (SJ), counter-movement jump (CMJ), standing jump with a 20 kg load ($SJ_{20\ kg}$), standing jump with a load corresponding to one-half body weight ($SJ_{1/2\ bw}$), and a 15-s rebound jump test (RJ). As described by Komi and Bosco (1978), standing jumps were performed with the subjects starting from a stationary semi-squatting position with 90° knee flexion. No counter movement was allowed with any body segment, and hands are kept fixed on the hips. In the counter-movement jumps the subjects started the movement from a stationary erect position with knees fully extended and they were then required to bend down to approximately 90° knee flexion before starting the upward motion of the jump. The 15-s rebound jump test consisted of continuous counter-movement jumps, where the subjects were encouraged to jump as high and as fast as possible for 15 s. Rebound jumping was also performed with hands fixed on the hips, and in each jump squatting down to approximately 90° knee flexion. In particular, care was taken to ensure that there was no counter-movement in the standing jumps and that the subjects landed with straight legs. The best out of three technically correct attempts was recorded and used for the statistical analysis, except for the 15-s rebound jump test, which was performed only once.

Paper IV. In the second biomechanical study, the players went through a standardized jump and power testing program. The testing program was performed using a contact mat connected to a computer (Intervall A/S, Oslo, Norway). The jumps performed were SJ, CMJ, $DJ_{45\ cm}$, $SJ_{20\ kg}$, $SJ_{1/2\ bw}$, $SJ_{1/1\ bw}$, and a RJ. $DJ_{45\ cm}$ was a drop jump from a dropping height of 45 cm. Otherwise the performance of the different jumps was the same as described in Paper III. In addition, during the execution of the $SJ_{1/2\ bw}$ and $SJ_{1/1\ bw}$ tests, average velocity, force and power during the jump were measured using the Ergopower system (Ergotest Technology AS, Langesund, Norway). The equipment measures the displacement of gravitational loads, in this case barbells, as external resistance (Bosco et al. 1995). The vertical displacements of the loads are monitored with mechanical and sensor arrangements. When the subject moves the loads, the signal from the sensor interrupts the microprocessor every 3 mm of displacement. Thus, it is possible to calculate

velocity, acceleration, force, power, and work corresponding to the load displacements. The system has been shown to be adequate in terms of its accuracy and reproducibility (Bosco et al. 1995).

Figure 2. Illustration of the experimental setup for the jump tests. During all tests the players jumped on a contact mat connected to a computer, making it possible to compute jumping height (Bosco et al. 1983).

Ultrasound examination

Ultrasonography was performed using a 7.5 MHz real-time, linear array probe (Model Sonoline SI 400, Siemens, Germany). A stand-off gel mattress was used to enhance the image. The players were scanned in a supine position with the knee in about 30 degrees of flexion to ensure an extended tendon (Kälebo et al. 1991, Fornage 1987). All ultrasound examinations were performed by an experienced ultrasonographer who was blinded to the patients' history and the results of the clinical examination. The patellar tendon was examined for any of the following

changes: Hypo- or hyperechoic zones, signal changes in the anterior surface or the posterior margin, and bursa appearance. Care was taken to hold the probe perpendicular to the tendon (Kälebo et al. 1991, Fornage 1987). The length of any hypoechoic zones was recorded. Prints of the images were also obtained for future reference.

The lengths of the patella and patellar tendon were measured using longitudinal scans. Similar to the Insall-Salvati index (Insall and Salvati 1971), an index of patella length to patellar tendon length was calculated. Finally, the proximal and mid-part width and thickness of the tendon were measured using transverse scans (Fig. 3). Assuming an ellipsoid shape, the proximal and mid-part cross-sectional areas of the tendon were calculated as: $\pi \times (W/2) \times (T/2)$, where W is the width and T is the thickness of the tendon.

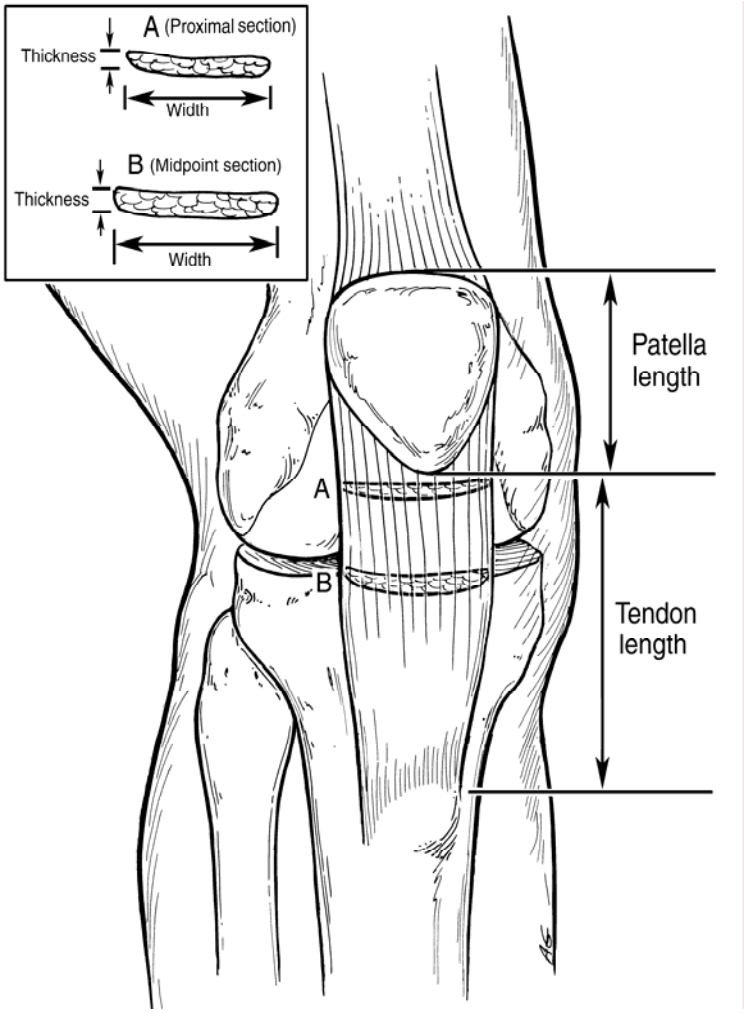


Figure 3. Measurements of patellar length, and patellar tendon length, width and thickness of the patellar tendon as made on ultrasound scans.

Immunehistochemistry

Surgical technique

The surgical exposure was identical in the two groups, the patient group with patellar tendinopathy and the control group with tibia fracture, with a straight medial or lateral parapatellar incision, splitting of the paratenon and exposure of the patellar tendon. In both groups the biopsies were taken with the proximal limit at the bone-tendon junction. In the control group the biopsies were taken with a width of at least five mm and a length of at least 20 mm from the middle portion of the tendon. In the patient group the biopsies were taken in the same manner, since the pathological tissue was confined to the middle and proximal part of the tendon. The biopsies were taken with full thickness of the tendon in the anterior-posterior direction.

Biopsy procedure

The biopsy handling was identical in the two groups. Immediately after the surgical procedure, the biopsies were transferred to Zamboni solvent (Zamboni and De Martino 1967). The biopsies were stored in this solution for 4-24 hours, and then washed in 0.1 M phosphate-buffered NaCl (PBS), pH 7.2, with 15% sucrose (weight/volume) and 0.1% natriumazide. The biopsies were then stored in PBS at 4 °C for a minimum of 48 hours. They were stored in this way for later immune-histochemical analyses.

Nerve staining and analyses

The samples were sectioned at 15 μm on a Leitz cryostat and frozen sections were mounted directly on Super-Frost/Plus glass slides and stained using the avidin-biotin or the haematoxylin-eosin systems, for immunohistochemistry and light microscopy, respectively.

Immunohistochemistry

The slides were rinsed for 10 min in PBS. Incubation with 10% normal goat serum in PBS for 30 min blocked nonspecific binding. Subsequently, the sections were incubated overnight in a humid atmosphere at +8C° with primary antisera for protein gene product 9.5 (PGP, 1:10000, Ultraclone, UK), a general nerve marker, substance P (SP, 1:10000, Peninsula Laboratories, USA) and tyrosine hydroxylase (TH, 1:5000, Peninsula Laboratories, USA), a rate-limiting enzyme

reflecting the occurrence of noradrenaline (NA). After incubation with the primary antisera, the sections were rinsed in PBS (3x5 min) and then incubated with biotinylated goat anti-rabbit antibodies (1:250, Vector Laboratories, CA, USA) for 40 min at room temperature. Finally, the sections were incubated for 40 min with Cy3-conjugated avidin (1:5000, Amersham International plc, UK). Control staining was performed by omitting the primary antiserum. A Nikon epifluorescense microscope (Eclipse E800, Yokohama, Japan) was used for the analyses. The occurrence of PGP, SP and TH was subjectively assessed and pictures were taken for subsequent semi-quantitative analyses.

Semi-quantitative analysis

After the subjective assessment, the following steps identified in an earlier study (Ackermann et al. 2002) were applied in order to optimize the semi-quantitative analysis: The patellar tendon biopsies were sectioned longitudinally and the sections were numbered consecutively from the dorsal to the ventral aspect. Three sections from different levels, i.e. ventral, middle and dorsal parts of the tendon were chosen to represent the full thickness of the tendon. Staining was performed simultaneously for all sections to be compared. For microscopic analysis, a video camera system (DXM 1200, Nikon) was attached to the epifluorescence microscope and connected to a computer. From each section, one image from the microscopic field (20x objective) exhibiting the strongest immunofluorescence was stored in the computer. Thereafter, the images were analyzed using the software Easy Analysis (Technooptik, Sweden). The software denotes and considers all positively stained nerve fibers beyond a defined threshold of fluorescence intensity. The results were expressed as the fractional area occupied by positive fibers in relation to the total area. The fluorescent/total area was determined in three images in each biopsy of the patient and control groups, respectively. In the microscopic analysis, the mean interobserver coefficient of variation was 9.8 % and the intraobserver variation was 9.6%. For statistical analysis, the mean fluorescent/total area was calculated for each of the ten biopsies from both the patient and the control group.

Apoptosis assessment

Light microscopic appearance

5 μm sections were routinely stained for H&E (general morphology) and Alcian Blue (sulphated glycosaminoglycans) and viewed at 100 to 630x magnification on a Zeiss Axioplan upright microscope.

Detection of apoptosis and assessment of caspase activation

Apoptosis was assessed using a monoclonal antibody against single-stranded DNA breaks (F7-26; Chemicon, Temecula, U.S.A.), as well as with a polyclonal antibody against the active (cleaved) form of caspase-3 (Asp 175; Cell Signaling), and propidium iodide staining (Sigma-Aldritch) for nuclear morphology. Of these methods, the cleaved caspase-3 antibody yielded the most specific and reproducible labeling of apoptotic cells in tonsil tissue (serving as a positive control), and was thus used for systematic quantification. The sections were cleared, quenched in 3% hydrogen peroxide, incubated in protein-free block for 15 min, then left overnight with the antibody diluted 1:50 in 0.1% bovine serum albumin in tris buffered saline (TBS). Slides were then sequentially exposed in a dark, moist chamber to horse radish peroxidase-conjugated goat-anti-rabbit (1:100, 30 min), fluorescyl-tyramide amplification reagent (DAKO Diagnostics, Glostrup, Denmark), anti-fluroescein-horse radish peroxidase, and finally 3,3'-diamino-benzidine (Vector Laboratories, Burlingame, U.S.A.) for 5', with 3x5' washes in TBS between each step. Bouin's fixed tonsil with or without the primary antibody was used as positive or negative control, respectively.

Image analysis

The identity of slides was masked with black tape. Using a 40x objective lens, the tissue section was illuminated with halogen or fluorescent light (488 nm wavelength) and respective areas of positive F7-26 or propidium iodide staining were captured at 1392 x 1045 pixels with a digital camera (Retiga Exi 1394, Qimaging Corp, Burnaby, Canada). For quantitation of apoptosis, fifteen random areas (0.30 mm^2 each) from the proximal region were digitized. Cells were considered positive only if the labeling was dense and suggestive of apoptotic morphology. A standard exposure time (50ms) was used through, and the contrast was not digitally adjusted.

Ethics

Study II, III, IV, V and VI were approved by the Regional Ethical Committee for Medical Research. In all six studies participation was voluntary and consent was obtained.

Statistics

In paper IV, in order to evaluate the performance ability of the leg extensors for each player a composite jump index was calculated by rating each player's result on a scale from 0 to 100 on each of the following jump tests: SJ, CMJ, CMJ-SJ, DJ, RJ, $SJ_{20\ kg}$, $SJ_{1/2\ bw}$ (power) and $SJ_{1/1\ bw}$ (power), where 0 represents the lowest test score among all the players tested and 100 the best score. The overall score was computed as the average of the results from each of these eight scores. Descriptive data are given as means ± SD and/or range unless otherwise noted. Comparisons of continuous data between groups were done using analysis of variance or unpaired t-tests, as noted in the results. Prevalence was compared between groups using Pearson chi-square tests. In paper IV proportions are reported with the corresponding SE, where relevant. In paper IV multiple logistic regression was used to test the effect of potential risk factors for jumper's knee (age, height, weight, experience at elite level, volume of sports specific training, weight training and jump training), adjusting for differences between sports. An alpha level of 0.05 was considered significant.

In Paper VI, for quantitation of apoptosis, the following variables were compared using caspase-3-labeled tissue sections; total number of positive cells in all areas, number of positive fields, average number of positive cells per field, and Apoptotic Index (% positive cells in all fields).

Results and discussion

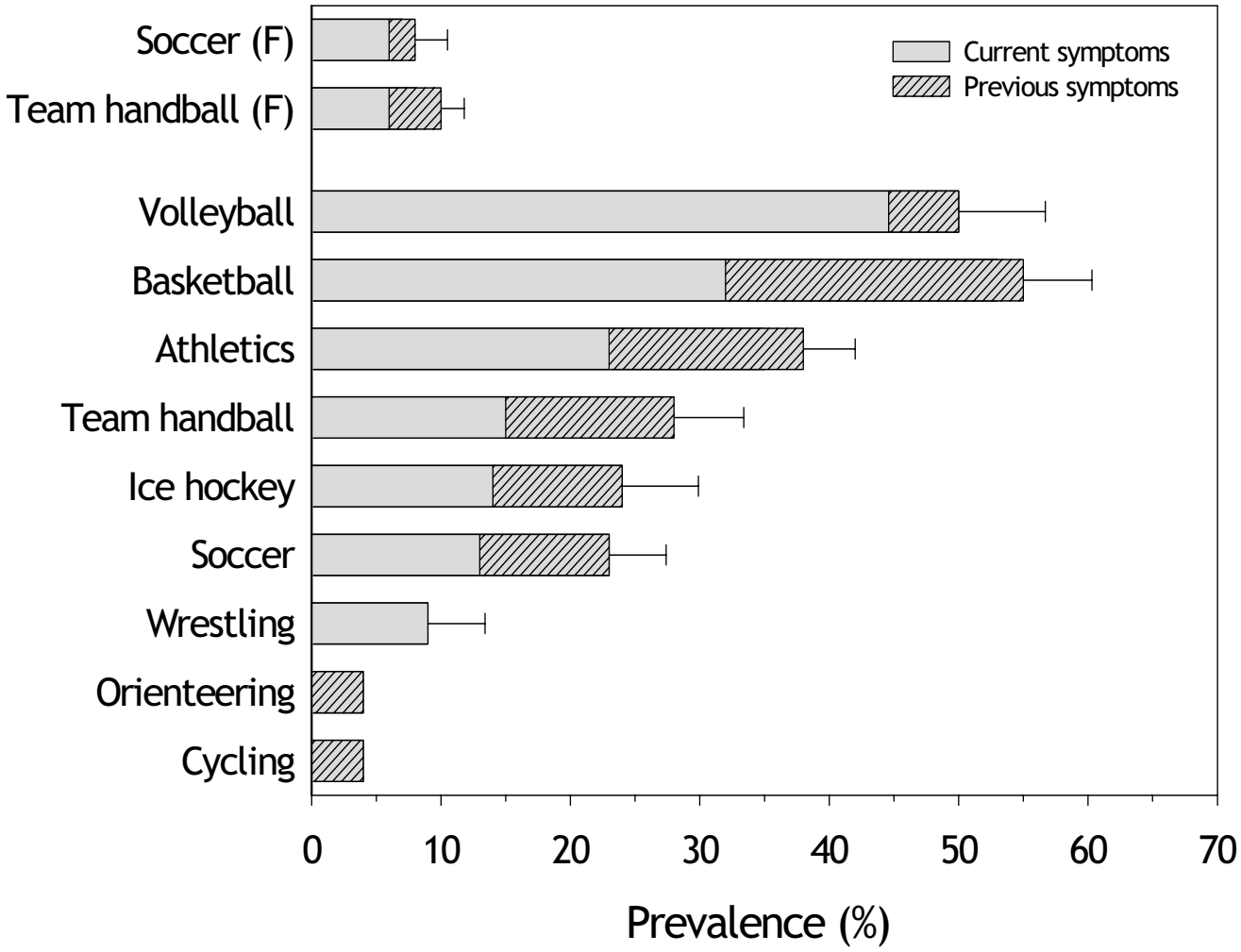
Prevalence data

Results

Paper I. The overall prevalence of current jumper's knee was 14.2±1.4% (87 of 613 athletes). Of the 87 athletes with current symptoms, 37 had bilateral symptoms, while 30 athletes had symptoms from the right side only and 15 players had symptoms from the left side only. This means that the prevalence of current jumper's knee affecting the right knee was 10.9% (67 players) and of the left knee 9.3% (57 players). In addition, 51 athletes (8.3%) reported previous symptoms of jumper's knee affecting one or both legs, resulting in a prevalence of current or previous symptoms of 22.5% (138 of 613 athletes). Only one athlete diagnosed with current jumper's knee localized the pain to the quadriceps tendon insertion at the upper patellar pole, the rest localized the pain to the patellar tendon.

As shown in Fig. 4, there were significant differences in the prevalence of current jumper's knee ($\chi 2$ test, $p<0.001$), as well as in the prevalence of previous symptoms ($\chi 2$ test, $p<0.001$). The prevalence of current symptoms was highest in volleyball with 44.6±6.6% and basketball with 31.9±6.8% while there were no cases in cycling or orienteering.

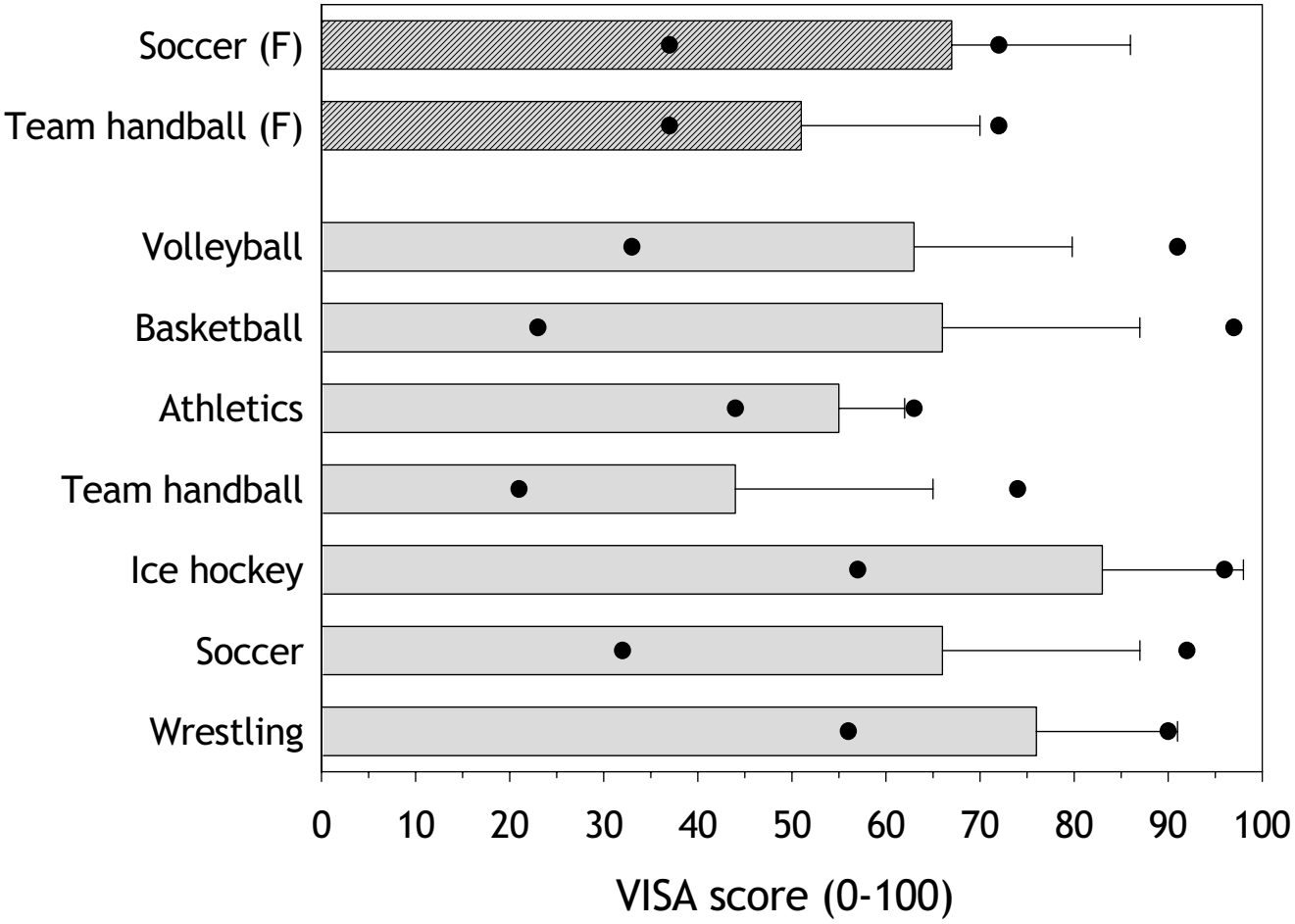
Figure 4. Prevalence (%) of current (white bars) and previous (hatched bars) symptoms of jumper's knee. The results for female athletes (F) are shown in the two upper bars, the rest of the results are for male athletes. Error bars denote SE.



The mean symptom duration among athletes with current jumper's knee was 32±25 months (range: 1-144 months, n=87). There was a significant difference in symptom duration between the different sports (ANOVA, p=0.04).

The mean VISA score reported across sports and genders was 64±19. As seen in Fig. 5, the VISA score reported by players with current symptoms of jumper's knee was significantly different between sports (ANOVA, p=0.003). The lowest VISA score was reported by male team handball players and the highest by ice hockey players.

Figure 5. VISA scores for players with current symptoms of jumper's knee in the various sports groups. For players with bilateral symptoms, the lowest value (worst knee) has been used. The top two hatched bars show the results for female athletes (F) from soccer and team handball, the open bars show the results for male athletes. No results are given for orienteering and cycling, since there were no athletes with current symptoms in these groups. The bars and error bars denote the mean and SD. In addition, the filled circles show the lowest and highest value in each group.



Paper III. In Paper III we examined 16 men's Division I and II teams with a total of 164 licensed players. Of these, 141 players participated in two tournaments in September 1989 just prior to the start of the indoor season and these players were interviewed during the tournaments. 55 players (38%) were diagnosed with current jumper's knee.

Paper IV. Of the 47 players participating in the study, 24 players (51.0%) were clinically diagnosed with current jumper's knee affecting at least one side. Twenty players (42.6%) had never experienced problems from any knee, whereas 3 players reported having had previous knee problems identified as jumper's knee (6.4%). The severity of symptoms among those with current jumper's knee (n=33 knees) was classified as grade I in 6 knees, grade II in 18 knees and grade IIIa in 9 knees. The onset of symptoms was gradual in 31 knees (94%) and acute in 2 knees, and

the duration of symptoms reported by the players with current complaints of jumper's knee was 3.5±2.4 (0.1-10) yrs. The age at symptom onset was 18.8±2.8 yrs (13.5-25.9).

Discussion

The main finding of Paper I was that the overall prevalence of jumper's knee was 14% across the sports included. In addition, 8% of the athletes reported previous symptoms, indicating that every fifth elite athlete is affected by jumper's knee during their athletic career. The prevalence varied between sports—from no cases in cycling and orienteering to 45% with current symptoms in male volleyball. In Paper III the prevalence of current jumper's knee was 38% and in Paper IV 51%. These prevalence figures probably represent *minimum* estimates since the athletes with the most serious problems, those who could not participate in training or competition, were not included in the studies. We do not know the number of athletes who were too disabled to be included. This may be a significant source of error, particularly in the individual sports, where it is more likely that an athlete would withdraw or not even enter the national championships if he thought that he could not perform fully. Also, an unknown number of athletes may have retired early because of jumper's knee, and some may have settled for a career on a lower level of performance because they could not tolerate the heavy training and competition load at the elite level. Thus, the elite samples we were able to study represent the survivors, and the true career prevalence is higher than that reported here as an overall result across the sports included.

It should also be noted that the mean duration of the symptoms was 32 months with a mean VISA score of 64. The information on the duration of the symptoms is based on memory, which means that the precision of this information is uncertain. Nevertheless, it seems clear that even with this limitation, there is no doubt that the majority of patients have played with symptoms for several years. This means that this condition can severely interfere with athletic performance, and even threaten an athletic career.

Another methodological limitation which must considered when interpreting the results is that the results are based on clinical examination alone, except in study II where we did an ultrasound examination. For practical reasons, we were not able to do MR or ultrasound imaging in the other studies to confirm the presence of structural tendon changes. This means that to be recorded as having current symptoms of jumper's knee, the athlete had to report a painful tendon during athletic activity with corresponding palpation tenderness. It may be argued that this definition is unspecific, since we do not know for certain that the tendon was the source of the pain in all cases. For instance, we could not rule out cases with referred pain, principally from the

distal aspects of the articular surface of the patella. In fact, a number of studies have shown that the correlation between clinical findings and ultrasound (Myllymäki et al. 1990, Cook et al. 2000a, Khan et al. 1997, Khan et al. 1999) or MR (Davies et al. 1991, Bodne et al. 1988, Khan et al. 1996) examinations is low, and even that symptoms and tendon changes come and go independently (Cook et al. 2000a, Cook et al. 2001). A significant number of athletes have or develop visible tendon changes without symptoms of jumper's knee and some have significant pain without detectable tendon changes (Cook et al. 2001). Thus, we would argue that the current clinical definition provides the most valid estimate for the prevalence of jumper's knee, since it will detect all players with tendon symptoms during athletic performance.

To our knowledge, there are no previous reports on the prevalence of jumper's knee across different sports, although a number of case series presenting the outcome after surgical treatment indicate that the majority of patients are from sports with high demands on speed and power (Karlsson et al. 1991, Raatikainen et al. 1994, Martens et al. 1982)

As expected, in the present study the prevalence was high in volleyball and basketball (55% reporting current or previous jumper's knee), sports characterized by high demands on speed and power. The maximal muscle force that can be generated eccentrically is 1.5-2.0 times higher than the maximal isometric force, and several-fold higher than maximal concentric force, especially at high speeds (Herzog 2000). Also, the ground reaction force is different between different tasks, ranging from 2.8 times body weight during distance running to 6 bw during jumping in volleyball and 10 bw in a long jump take off (McNitt-Gray 2000).The highest ground reaction forces are seen with ballistic drop jumps, and the resulting forces through the extensor tendons are proportional to the ground reaction force. Therefore, it is reasonable to suggest a connection between the loading pattern of the knee extensors and the prevalence of jumper's knee. This seems to match the prevalence distribution seen in the present and previous studies, with the highest in basketball and volleyball (high jump volume and eccentric load), then athletics (sprinters and jumpers, high load, but less volume), followed by team handball, soccer and ice hockey (less jumping, some sprinting) and low prevalence among orienteerers (high volumes of running, but no sprinting) and road cycling (high volumes of concentric work, no ballistic loading).

Gender

Results

Paper I. The prevalence of current jumper's knee was lower among women with 5.6±2.2% (6 of 107 team handball and soccer players) compared with a combined prevalence of 13.5±3.0% (18 of 133) in the corresponding male sports (χ^2 test, p=0.042). However, there was no difference (t-test, p=0.48) in the duration of symptoms between female (22±12, n=6) and male athletes (28±21, n=55). Also, there was no gender difference in VISA score. The VISA score in female team handball and soccer was 59±15, compared with 58±23 in the same male sports (ANOVA, p=0.9).

The number of years of participation in organized training was 15.2±5.1, with 6.1±4.2 years at the elite level. The number of hours with sport-specific training was 11.8±3.9. There was no significant gender difference in these variables between athletes with current jumper's knee and those without.

Discussion

Gender as a risk factor for jumper's knee had not been studied before in contrast to acute knee injuries, particularly ACL tears (Myklebust et al. 1998, Arendt and Dick 1995). The prevalence of current symptom was 5.6% among female team handball and soccer players compared with 13.5% in the corresponding male sports. The question is what the cause of the apparent gender difference is. We chose team handball and soccer to examine the gender difference, since these are sports which in Norway are played at an equally high performance level by men and women, where we therefore thought player experience and training volumes would be similar. Also, we expected a relatively high prevalence of jumper's knee in these sports. As seen from Table 4 in Paper I, the training volumes (15-17 h/week total training time) and background (15-18 years of organized training, 5-7 years at the elite level) were similar between men and women. The difference in prevalence may be attributed to a number of other factors. It is well documented that the jumping ability and force-generating capacity is lower among women than men (McNitt-Gray 2000). So, even if the number of sprints and jumps may be similar between men and women playing the same sports, the lower prevalence may simply reflect that the forces that are transmitted through the quadriceps and patellar tendons are lower among women.

Antropometrical data

Results

In Paper I athletes with current jumper's knee weighed more (83.6 kg±11.6 vs. 77.3 kg±11.9, p<0.001) and were taller (186±9.5 cm vs. 181±9.2 cm, p<0.001).

In male soccer the jumper's knee group was significant taller than the others (186 ±4.3 cm vs.183 ±5.5 cm, p=0.05). Otherwise, there were no other significant differences between those with jumper's knee compared with those without within each sport with regard to age, height and weight. In a logistic regression model which included gender, sport, age, height, weight, training background, and the volume of the different types of training, only weight training and jump training were significant factors.

In Paper III there was no difference between the groups with regard to age, height and weight.

In Paper IV players with jumper's knee had a significantly higher body weight than the controls, but there was no difference in height and age.

Discussion

Age was not a significant risk factor for jumper's knee in any of the present studies. Among volleyball players there was no significant difference in height between players with jumper's knee compared with controls. In the overall material in Paper I (prevalence study), the athletes with jumper's knee were significantly taller, but within each specific sport there was only significant difference in height among male soccer player. In a logistic regression model which included gender, sport, age, height, weight, training background, and the volume of the different types of training, only weight training and jump training were significant factors. As a conclusion, height is not a significantly associated risk factor for jumper's knee. In Paper I and IV athletes with jumper's knee were significantly heavier than those without jumper's knee. We did not examine body composition, but it seems unlikely that the body weight difference observed was due to differences in body fat in such a well-trained population of players. The players with jumper's knee reportedly trained significantly more with weights than the others in study II and IV. This weight training by itself means a higher total loading of the extensor apparatus, and the anticipated effect of this training is also to increase muscle mass and jumping ability.

Sports history and training background

Results

Paper I. The number of years of participation in organized training was 15.2±5.1, with 6.1±4.2 years at the elite level. The number of hours with sport-specific training was 11.8±3.9. There was no significant difference in these variables between athletes with current jumper's knee and those without. However, athletes with current jumper's knee did significantly more weight training (3.5±2.4 h/week vs. 2.5±2.1, $p<0.001$) and jump training (1.1±1.8 h/week vs. 0.5±1.0, $p<0.001$).

The comparison between athletes with current jumper's knee and those without within each specific sport showed that in basketball, the athletes with jumper's knee did significantly more sport-specific training than those without jumper's knee (14.7±2.7 h/week vs. 12.3 ±2.5 h/week, $p=0.005$). In male handball the athletes with jumper's knee did significantly more plyometric training compared with those without jumper's knee (0.7±1.0 h/week vs. 0.2±0.3 h/week, $p=0.01$). In a logistic regression model which included gender, sport, age, height, weight, training background, and the volume of the different types of training, only weight training and jump training were significant factors.

Paper III. In this study the players with jumper's knee did a significantly higher number of weekly training sessions compared with the athletes without jumper's knee. There was no difference between the groups with regard to number og seasons played, weight training, jump training, warm-up time or stretching time.

Paper IV. The characteristics of the players and their training background are shown in Table 2. The prevalence of current jumper's knee was significantly higher among outside hitters (68%) and middle blockers (64%) compared with utility players (28%) or setters (18%).

*Table 2. Characteristics of players with current symptoms of jumper's knee (n=24), and without history of jumper's knee (n=20). Values are means ± SD. *Significantly different from players without history of jumper's knee (unpaired t-tests).*

	Current jumper's knee	No history of jumper's knee	Significance level (p)
Organized volleyball training (yrs)	8.0±2.8	7.5±3.6	0.55
Training at senior level (yrs)	6.8±2.5	5.7±3.6	0.28
Training at elite level (yrs)	2.5±2.6	2.2±3.2	0.70
Volleyball training (h/wk)	7.7±2.1	7.4±1.6	0.53
Weight training (h/wk)	4.5±2.8*	2.3±2.3	0.009
Jump training (h/wk)	0.4±0.9	0.6±1.1	0.53
Sum training (h/wk)	12.6±4.2	10.3±3.9	0.06
Stretching during warm-up (min)	3.4±3.0	3.1±2.7	0.71
Stretching after training (min)	6.2±5.8	7.1±3.9	0.55

Discussion

Epidemiological studies on extrinsic factors have shown that the hardness of the playing surface and an increased frequency of training sessions correlate positively with the prevalence of jumper's knee (Ferretti et al. 1984, Ferretti 1986). This is supported by the results in Paper I, which shows a small, but significant difference in training volume between players with and without symptoms. In Paper II we found no difference between the groups in the total amount of specific volleyball training, since all the players were selected from a well-trained group with a similar training history. In Paper I, athletes with jumper's knee did significantly more jump training. In the same study the sport with the highest prevalence of jumper's knee was basketball (55% reporting current or previous jumper's knee), a sport characterized by high demands on speed and power. In this sport, athletes with current jumper's knee did significantly more sport-specific training than those without jumper's knee. In other words, there is substantial evidence to suggest a link between the total load on the tendon and the prevalence of jumper's knee.

Volleyball involves approximately 60 maximal jumps per hour of play, and previous studies have shown that the prevalence of jumper's knee increases with increased frequency of training (Ferretti et al. 1984, Neri 1991). The tactics of the game require middle blockers jump more than others, and it has been shown that they have a higher prevalence of jumper's knee (Neri 1991). We did find that the prevalence of jumper's knee was significantly higher among outside hitters and middle blockers compared to utility players and setters. This is not surprising, since outside

hitters and middle blockers perform a much higher number of maximal jumps than setters as a result of their function on the team. In line with this, it has recently been shown that the prevalence of jumper's knee among elite beach volleyball players is only 9%, considerably lower than in indoor volleyball players (Bahr and Reeser 2003). The explanation for this difference in prevalence is probably that jumping and landing in soft sand is less demanding on the tendon than is jumping on indoor playing surfaces. Thus, there is reason to suggest that the prevalence of jumper's knee in volleyball players is closely related to the volume of jumping and playing surface hardness.

The players with jumper's knee reportedly trained more with weights than the others (Paper I and IV). In Paper I, a logistic regression model which included gender, sport, age, height, weight, training background, and the volume of the different types of training, only weight training and jump training were significant factors. This weight training by itself means a higher total loading of the extensor apparatus, and the anticipated effect of this training is also to increase muscle mass and jumping ability. This is supported by the fact that the players with jumper's knee had a higher body weight than those without jumper's knee.

However, in the present studies we do not have detailed information on the training history of the players at the time they were first injured. At that time there may have been differences in e.g. training volume or intensity that we were unable to detect in a cross-sectional study, and longitudinal studies are necessary to examine in detail how training programs may lead to tendon overload.

Biomechanical data

Results

Paper III. The players from the patient and control groups came from the same teams, used the same type of shoe, and trained and played on the same type of gym floor. The characteristics of the patient group and the matched control group who underwent the jump testing program are shown in Table 3.

*Table 3. Characteristics of patient group (n=12) and control group (n=12). Values are means ± SD. *Significant difference between groups.*

	Patient group	Control group
Age (yrs)	23.7 ± 3.0	24.8 ± 4.6
Height (cm)	189.3 ± 7.0	187.9 ± 4.9
Weight (kg)	*84.1 ± 5.6	79.2 ± 3.7
No. of seasons played	7.2 ± 2.2	8.5 ± 2.8
No. of training sessions per week	4.6 ± 1.2	4.3 ± 1.1
Weight training (h/wk)	1.0 ± 1.0	1.0 ± 0.6
Jump training (h/wk)	0.3 ± 0.7	0.5 ± 0.5
Warm-up time (min)	19 ± 7	20 ± 3
Stretching time (min)	6 ± 4	5 ± 3

In the jump tests the patient group performed better than the control group in the counter-movement jump, the standing jump with a 20 kg load, and the 15-second rebound jump test. Also, the work done in counter-movement and standing jump was greater in the patient group, as was the difference between jump height in counter-movement and standing jumps.

Paper IV. The jumper's knee group scored significantly higher than the control group on the composite jump score (50.3 vs. 39.2, p=0.02), and significant differences were also observed for work done in the drop jump, and average force and power in the standing jumps with half and full body weight loads.

Thirty-seven players (79%) reported using a right-left step-close takeoff technique in the spike jump, whereas 10 players (21%) used a left-right takeoff. Only one player reported preferring the right leg when landing after the attack, whereas 31 players (66%) reported a balanced landing technique, and 15 players (32%) reported favoring their left leg when landing. The takeoff and landing techniques among the players with current jumper's knee are shown in Table 4.

Table 4. Takeoff and landing technique in spike jump among players with current jumper's knee on the right and left side.

	Right knee (n=22)	Left knee (n=11)
Right-left takeoff	20	11
Left-right takeoff	2	0
Right-left landing	0	0
Left-right landing	6	4
Simultaneous landing	16	7

Discussion

The main finding of these studies was that the groups of players with jumper's knee performed better in standardized series of jump and power tests compared with the control groups.

Dynamic characteristics such as jumping capacity and loading of the extensor mechanism are by definition possible intrinsic predisposing factors for jumper's knee. However, data on intrinsic disposing factors for jumper's knee is limited and it is not known why some players have problems, whereas others do well despite almost identical external predisposing factors, such as high training and jumping volumes. There is no convincing evidence in support of suggestions that injury may be associated with malalignment of the extensor mechanism of the knee, patella alta, abnormal patella laxity or other structural abnormalities (Ferretti et al. 1984, Ferretti 1986, Kujala et al. 1986, Kujala et al. 1989, Kujala et al. 1987, Torstensen et al. 1994). However, the problem may be related to the performance characteristics of the leg extensors. Players who jump well load their tendons more than others and this may lead to a greater risk of injury. Our data seem to indicate that this is the case, because the patient group in both studies performed better compared with the control group.

In Paper III it is interesting to note that the test results did not differ between the groups for all modes of jumping. The standing jump is designed as a "pure" concentric movement, and the results for unloaded jumping did not differ between the groups. However, for the counter-movement jump, which consists of a ballistic movement of a rapid eccentric muscle action immediately followed by a maximal concentric contraction, there was a significant difference between the groups. We also observed a significant difference in the 15-second rebound jump test, which consists of a series of ballistic jumping movements. Consequently, it may be suggested that the main difference between the groups could be the way in which they were able to utilize the eccentric pre-stretch component of the ballistic motion to increase their jumping height.

However, we could not reproduce these results in Paper IV. Paper III included a smaller number of players, and in a case-control study it is possible that a selection bias may have occurred. However, the performance of the players with jumper's knee in Paper III in the counter-movement jump test and the rebound jump test was significantly better than the results of the players in Paper IV. This suggests that the injured players in the first study had a highly developed leg extensor apparatus, which may implicate a stronger predisposition towards jumper's knee.

The right knee was affected twice as often as the left knee (Paper IV). The majority of the players used a right-left step-close takeoff technique, and none of the players reportedly preferred the right leg when landing after the attack. In fact, 20 of the 22 players with current jumper's knee on the right side used a right-left takeoff technique. This suggests that a relationship may exist between the takeoff technique and jumper's knee, and that the forces sustained during takeoff may be of considerable importance. In order for a right-handed player to obtain proper alignment of the upper body for an effective spike, the preferred technique involves placing the right foot first and about 45º externally rotated (Selinger and Ackermann-Blount 1986). When using this takeoff technique, the deceleration work is mostly done with the right leg, subjecting it to higher eccentric loading than the left leg. Also, when these high loads are imposed, the right leg may be in a state of functional malalignment. The preferred takeoff technique results in a valgus position of the right leg, a greater flexion angle of the knee, as well as external rotation of the tibia relative to the femur. It is possible that these factors result in a more unfavourable loading pattern of the right knee with respect to development of jumper's knee. Motion analysis and direct force measurements are necessary to study this phenomenon in more detail. Based on the present studies there is reason to suggest an overall better jumping capacity, especially in jumps with an eccentric component, as important intrinsic predisposing factors for jumper's knee.

For the injured athletes to have been able to jump higher than the control subjects, a larger vertical impulse must have been produced. Force was not measured directly in Paper III, but it is likely that the force transfers through the patellar tendon were larger as well. From previous studies of volleyball players, it is known that good jumpers are characterized by a shorter contact time and higher peak force during take-off (Selinger and Ackermann-Blount 1986). Thus, the difference in peak force is likely to be larger than the difference in the jump result alone would seem to indicate. Since more than 50% of the work done in jumping is produced by the knee extensors (Luhtanen and Komi 1978), it seems reasonable to conclude that the differences

observed in jumping height reflects a true increase in the force transfer through the patellar tendon.

The jumping ability of the players, 40-45 cm in a counter-movement jump, may not seem impressive. However, the jumping mode tested differs from the techniques used when playing volleyball. In a spike jump players usually employ an approach run of two steps, a step-close take-off technique and a full arm swing, thereby adding another 55-65% to their counter-movement result (Bahr et al. 1992). There is a close correlation between the results of a counter-movement jump and a spike jump (r=0.96) (Bahr et al. 1992), and based on this relationship the spike jump of this group of injured players may be estimated to range from 55 to 92 cm. The forces involved during take-off and landing are also larger than during the standard test situation used in the present study (Bahr et al. 1992).

In Paper IV the composite jump index was designed as an overall indicator of a player's ability to load the extensor apparatus during conditions ranging from slow-speed concentric (standing jump with added load) to high-speed ballistic (rebound jumps). The dynamic testing program was selected to resemble the various loading conditions imposed on the leg extensors during different jumping and cutting movements used in the game of volleyball. The significant difference observed between the groups in the composite jump index may be taken as an indication that the leg extensor apparatus in the group with jumper's knee may be subjected to higher loads during volleyball play, as well. There were significant differences between the players with current jumper's knee and those without both in average force and average power in standing jumps with added loads corresponding to one-half and whole body weight. Consequently, the forces acting on the tendon or the rate of force development during jumping may surpass the adaptive abilities of the tendon.

The study designs have some limitations which must be borne in mind when interpreting the results. It is possible that the selection of athletes to the patient group was biased, since diagnostic criteria were based on a typical history and clinical findings alone. However, we included only athletes with a typical history of patellar tendon pain in the patient group, and care was taken to exclude athletes with evidence of additional or other pathology. In Paper III the matching of the control players from the same teams based on age, function, playing experience and training level was felt to be the best way to minimize the risk of a selection bias. While the study format allowed us to match the patient and control groups carefully with respect to diagnosis and factors believed to be of importance in the development of jumper's knee, it also

resulted in a small sample size, and the results therefore needed to be validated in a larger population of athletes as in Paper IV.

The jump testing protocol is a standard program which has been shown to be highly reproducible (Sale 1990). The tests are functional, designed to give an estimate of performance at different speeds and loads, much in the same way that different demands are placed on the leg extensors for given tasks during the actual game of volleyball. The tests were familiar to the examiners as well as many of the teams, who use the same tests on a regular basis to check the efficacy of their training programs. Pain inhibition during jump testing among the players in the patient group is possible. The players did not express any problems and even if this occurred, it would appear not to invalidate the results, since the patient group still performed better than the control group.

An interesting observation in this connection is that athletes with longstanding complaints from what is supposed to be an overload condition perform better in dynamic tests with high resemblance to the movements and loading mechanisms of the extensor apparatus which is supposed to be the reason to the injury compared with asymptomatic athletes. However, whether the athletes with jumper's knee actually have reduced performance level compared with their preinjury level or not can only be answered through longitudinal studies. Since the athletes with jumper's knee perform better compared with controls in dynamic testing procedures even with serious symptoms for many years we can not explain their reduced performance level by reduced performance of their extensor mechanism. The problems the athletes with reports are correlated to their experiences of pain. This means that there is reason to suggest a connection between a high jumping capacity and high training volumes and the pain mechanisms within the tendon. It is also reason to suggest a correlation between an overload condition giving specific histopathological changes that can explain the pain mechanisms since the histopathological findings are consistent and uniforme (Roels et al. 1978, Karlsson et al. 1991, Colosimo and Bassett 1990, Bassett et al. 1980, Khan et al. 1998).

Ultrasound data

Results

Paper II. Palpation tenderness was found in a number of players who did not complain of symptoms of jumper's knee, and the predictive value of pain on isometric contraction was low (Table 5). Previous Osgood-Schlatter's disease was reported in 2 cases among those with current jumper's knee (34 knees), and in 8 of 60 knees without current symptoms (n.s.)

Table 5. Clinical findings in 34 knees with current jumper's knee and 51 knees without symptoms. Knees with previous symptoms (n=9) only were excluded from the analysis.

Test	Test result	Current symptoms (n=34)	No symptoms (n=51)
Palpation tenderness	Negative	-	39
	Slight	9	6
	Moderate	12	6
	Strong	13	-
Pain on isometric contraction (0°)	No	24	48
	Yes	10	3
Pain on isometric contraction (30°)	No	29	51
	Yes	5	-
Pain on isometric contraction (90°)	No	31	51
	Yes	3	-
Chondromalacia tests	Negative	27	43
	Positive	7	8

Tendon changes observed by ultrasonography

Table 6. Dimensions of the patellar tendon and patella in athletes with (n=30 knees) or without (n=51) current symptoms of jumper's knee. Knees with previous symptoms or symptoms from the quadriceps tendon only were excluded from the analysis (n=13). Values are means ± SD.

	No symptom	Current symptoms	Significance level (P)*
Tendon length (mm)	52±5	53±7	0.29
Patella length (mm)	38±3	39±3	0.79
Insall-Salvati index	0.75±0.10	0.73±0.08	0.46
Proximal thickness (mm)	3.8±1.1	6.2±2.2	<0.001
Proximal width (mm)	33±3	33±4	0.65
Proximal area (mm)	99±29	161±60	<0.001
Midpoint thickness (mm)	3.9±0.7	4.1±0.5	0.21
Midpoint width (mm)	36±3	37±6	0.003
Midpoint area (mm2)	108±20	120±19	0.08

**Unpaired t-test.*

The degree of clinical symptoms could not be reliably predicted from the changes observed in paratenon appearance or by the presence of hypoechoic changes. The length of the hypoechoic zone was 11.5±4.2 mm among those without symptoms, and 10.0±0.0 mm, 14.4±2.8 mm and 20.1±8.4 mm among those with grade I, II and IIIa symptoms, respectively (n.s., ANOVA).

No increase was observed in proximal tendon thickness or length of any echoic changes observed in relation to the duration of current symptoms of jumper's knee.

Discussion

The main finding of this study was that the prevalence of jumper's knee and ultrasound changes in the patellar tendon was high, approximately 50%, but that the correlation between symptoms and ultrasound changes was low. In the present study, 7 of the 30 knees with a clinical diagnosis of jumper's knee in the patellar tendon had normal ultrasound findings. On the other hand, we found ultrasound changes believed to be associated with jumper's knee (tendon thickening, echo signal changes, irregular paratenon appearance) in 12 of 51 knees without current or previous symptoms.

The findings in the present study have later been confirmed by others. In a cross-sectional cohort study by Cook et al. (1998), they assessed the sonographic patellar tendon appearance in 320 athletes from different sports (basketball, cricket, netball and Australian rules football) without any current or previous complaints compatible with jumper's knee compared with 27 nonathletic individuals as controls. In the asymptomatic group of athletes they found hypoechoic changes in the tendon in 22% and in 4% in the control group, in 30% of male and 14% of female athletes without symptoms, and in 32% of asymptomatic basketball players compared with 9% in the other sports (all $p<0.05$). In another study by Cook et al. (2000b) they studied the patellar tendons in 134 elite 14- to 18-year old female (n=64 and male (n=70) basketball players and 29 control swimmers (17 female and 12 male) clinically and ultrasonographically. Of tendons categorised clinically as "never patellar tendinopathy", 22% had an ultrasonographic hypoechoic region.

To evaluate the ability of ultrasonography to predict eventual symptoms Khan et al. (1997) compared patellar tendon sonographic findings at baseline and at follow-up in female basketball players with and without symptoms of jumper's knee. They concluded that patellar tendon sonographic hypoechoic areas can resolve, remain unchanged or expand in active sports-women without predicting symptoms of jumper's knee. Cook et al. (2000a) did a longitudinal study on 52 elite junior basketball players with an ultrasonographic evaluation at baseline and after 16 months. All tendons were asymptomatic at baseline and 10 had hypoechoic changes at baseline and 42 were ultrasonographically normal at baseline. The relative risk for developing symptoms of jumper's knee was 4.2 greater in case tendons than in control tendons. Half of the abnormal tendons in women became ultrasonographically normal in the study period. Based on their data

they suggest that the presence of an ultrasonographic hypoechoic area is associated with a great risk of developing symptoms of jumper's knee. They concluded that neither qualitative nor quantitative analysis of baseline ultrasonographic images made it possible to predict which tendons would develop symptoms or resolve ultrasonographically. In another study by Cook et al. (2001), they used a longitudinal study design to examine whether or not the presence of a hypoechoic lesion in an asymptomatic patellar tendon conferred a risk for developing jumper's knee compared with a tendon that was ultrasonographically normal. They followed 46 patellar tendons over 47 ± 12 months. Eighteen tendons had hypoechoic changes at baseline and 28 were ultrasonographically normal. Five tendons resolved ultrasonographically in the study period. Seven normal tendons at baseline developed hypoechoic changes but only two became symptomatic. Analysis of ultrasonography at baseline and clinical outcome showed that there was no association between baseline ultrasound changes and symptoms at followup. There was no statistical significant relationship between ultrasonographic patellar tendon abnormalities and clinical outcome in elite male athletes. As a conclusion from the available studies there is ample evidence to state that the relationship between symptoms and clinical findings of jumper's knee and the ultrasound changes is weak.

Several authors have described the histopathological changes in the patellar tendon obtained from surgical specimens in patients with disabling jumper's knee, and their observations usually include tearing of tendon fibers, regeneration with fibroblast proliferation, myxomatous degeneration, and capillary proliferation without any inflammatory response (Roels et al. 1978, Karlsson et al. 1991, Colosimo and Bassett 1990, Bassett et al. 1980, Khan et al. 1998). However, these observations are from patients with disabling symptoms (grade IIIb), among whom conservative treatment methods have failed. The correlation between ultrasound findings and histopathology in patients with patellar tendinopathy has been studied by Khan et al. (1996). In this study, 28 knees diagnosed with patellar tendinopathy planned for surgical treatment underwent an ultrasonographic examination. Control biopsies were taken from 39 cadaver knees. All knees diagnosed with patellar tendinopathy had an ultrasonographically abnormal zone at the proximal patellar tendon and histopathological examination revealed mucoid degeneration in all these tendons and in three of 39 (8%) in the cadaver knees. This study correlates the histological findings in biopsies from patients clinical diagnosed with patellar tendinopathy combined with simultaneous typical ultrasonographic findings, and describes a very close correlation between this subgroup of athletes with patellar tendinopathy and a specific histopathologic finding (mucoid degeneration). All the previous mention studies on histopathology present results from a

cohort of patients with disabling symptoms (grade IIIb), among whom conservative treatment methods have failed.

However, to our knowledge, there is no available information on the histopathological changes in patients with Roels' grade I, II or IIIa disease. In spite of lack of this information, attempts have been made to correlate ultrasound changes and anatomical findings to the clinical staging of the disease (Fritschy and DeGautard 1988, Jerosch et al. 1990). Jerosch and Schröder (1990) suggested that a relationship exists between the severity of the pathological changes and certain ultrasound characteristics. More serious disease is assumed to be associated with wide-spread thickening of the tendon, echoic changes and surface irregularities. The correlations made in these studies are based on assumptions since the ultrasound findings are not correlated to corresponding histopathologic findings in the same individuals. In the present study we found no correlation between the presence of surface changes suggesting paratenon pathology, and either the presence of symptoms or the degree or duration of symptoms. This suggests that paratenon changes do not necessarily constitute a sign of more serious clinical disease.

Several studies have shown near-perfect correlation between preoperative ultrasound changes and surgical findings (Raatikainen et al. 1994, Orava et al. 1986, Kälebo et al. 1991, King et al. 1990, Karlsson et al. 1992). However, as these studies were carried out in a selected patient group, i.e., almost all of them had disabling symptoms (grade IIIb) who did not respond to non-operative treatment, the results should be interpreted carefully when applied to other patient populations. Indeed, the results of the present study and that of Myllymäki et al. (1990) show that the correlation between ultrasound changes and symptoms is weak among athletes with less serious symptoms. Karlsson et al. (1992) studied 91 patients with grade III symptoms and hypoechoic changes on ultrasound examination. When the patients were grouped according to the length of the hypoechoic zones, only 6.6% of the patients with changes of <10 mm needed surgical treatment, whereas 38.5% of those with changes of >20 mm subsequently needed surgical treatment (Karlsson et al. 1992). This suggests that the length of the hypoechoic zone may be a significant factor in planning treatment. However, we did not find any correlation between clinical staging and the length of the hypoechoic changes, nor could we find any relationship with the duration of symptoms. Since there appears to be a correlation between the size of the hypoechoic area and the effect of nonoperative treatment, but no correlation between size and clinical staging or duration of symptoms, this may be one reason why the relationship between clinical stage and effect of non-operative treatment may be difficult to predict. As a

conclusion from the present study specific ultrasound findings could neither be used to predict the clinical grade of the disease, nor the duration of symptoms.

When comparing normal tendons and tendons with symptoms of jumper's knee, we found a significant difference between the asymptomatic and symptomatic players in antero-posterior tendon thickness, particularly in the proximal part of the tendon, the location where most of the echoic changes were observed. Several studies involving surgery have found that in the majority of the cases the pathological process is localized in the proximal posterior part of the tendon (Roels et al. 1978, Ferretti 1986, Karlsson et al. 1991, Colosimo and Bassett 1990, Bassett et al.1980). MRI studies have shown that the antero-posterior diameter of the normal tendons increases slightly from proximal to distal (el-Khoury et al. 1992). Since stress/strain resistance is correlated to the cross-sectional area, this may explain why the pathological process usually starts in the proximal part of the tendon. The length of tendon fascicles varies with longer anterior fascicles than the corresponding posterior fascicles since the anterior bundles are attached more proximal to the patella and more distal to the tibia than the corresponding posterior bundles (Basso et al. 2001). For a same amount of elongation, the shorter posterior fascicles strain more than the longer anterior fascicles (strain=elongation/gauge length) (Basso et al. 2002), which may explain why the pathological process is localized to the posterior part of the tendon.

No difference in the tendon length or the modified Insall-Salvati index could be detected between symptomatic and asymptomatic groups of knees. This suggests that players with longer tendons are not predisposed to jumper's knee in contrast to Kujala et al.(1986, 1987), who reported a significantly higher proportion with patella alta among those with jumper's knee compared to controls. However, their reports included much fewer volleyball players in the control groups than in the patient groups, and this fact may have skewed their results and reduced the external validity of their studies.

Innervation

Results

Patient characteristics. The mean age was 30 years (24-34 years, n=10) in the patient group and 29 years (19-43 years, n=10) in the control group. In the patient group, the mean number of years participating in organized training was 17 (10-28 yrs, n=10), and the mean number of total training hours per week was 14 (6-24 h, n=10). The mean VISA score was 42 (15-65, n=10), and the mean duration of symptoms was 36 months (5-120 months, n=10).

Microscopy

The morphologic appearance of the painful tendons in the tendon proper differed significantly compared to the controls. The proper tendinous tissue exhibited signs of tendinosis (collagen degeneration, fiber disorientation, hypercellularity, angiogenesis, and absence of inflammatory cells) in all but one of the patients, whereas only a few of the controls exhibited early signs of tendinosis.

Semi-quantitative assessment of tenocyte morphology and of angiogenesis was performed according to the Bonar scale (Cook et al. 2004). Tenocyte changes occurred in all but one of the painful tendons, whereras only 5 of 14 controls exhibited these changes ($p=0.006$). Angiogenesis, considered to be the last histological sign of tendinopathy (Cook et al. 2004), was found in 4 of 11 painful tendons, but in none of the controls ($p=0.038$).

Immunohistochemistry

Overall, the subjective immunohistochemical assessment confirmed the morphologic appearance. However, it also provided more detailed information about sensory (SP) and sympathetic (TH) nerve fiber occurrence in the patellar tendon. Thus, the majority of the painful tendons exhibited an increased number of nerve fibers positive to SP and notably decreased levels of TH.

Sensory nerves

Closer subjective analyses showed that the increased number of SP-positive fibers in the painful tendons occurred mainly as thin, varicose, non-vascular nerve terminals within the tendon proper. Notably, these SP-positive nerves in the painful tendons were found over a larger area, more spread out within the tendon than in the controls. The SP positive nerve fibers seen as free nerve endings interspersed between the proper collagen fibers, often accompanying the loose connective tissue ingrowth within the tendon proper of the painful tendons. Contrary to what one might have expected, no differences were noted between the groups regarding the small subpopulation of vascular SP-positive fibers. In both groups, SP was regularly seen in larger nerve bundles.

Sympathetic nerves

Subjective analyses demonstrated not only a great difference in the occurrence of TH-expressing nerve fibers between patients and controls, but also in their morphological distribution. In both

groups, TH-positive nerves were present as free nerve endings throughout the tendon proper but, unlike the sensory nerves, the majority of the TH-nerves were distinctively related to the blood vessels. In the patients, there was a distinct decrease in the occurrence of TH-positive nerves. Some TH-positive free nerve endings were still seen, but the vessel-related TH nerves were significantly diminished in the patients.

General nerve occurrence

The neuronal localisation of SP- and TH-staining was confirmed by positive immunoreactivity for PGP, a general nerve marker. The subjective analyses of PGP showed a higher nerve fiber occurrence in the chronic pain group compared to the controls. Nerves existed both as vascular and non-vascular free nerve endings and in larger bundles.

Semi-quantitative immunohistochemistry

Computerized image analysis of SP, TH and PGP expression showed similar differences in occurrence as assessed subjectively, although all results were not statistically significant. The occurrence of SP was 22% ($p=0.567$) and that of PGP 54% ($p=0.098$) higher in the chronic painful tendons than in the controls. The occurrence of TH in the chronic painful tendons was 53% lower than in the controls ($p =0.018$).

Discussion

This study demonstrates that nerve fibers expressing sensory (SP) and sympathetic neuromediators (TH) appear to differ between patients with painful patellar tendinopathy and healthy controls. Most notably, an increased number of SP-positive non-vascular nerve endings and a vascularly related decrease in TH were seen.

The sensory neuropeptide, substance P, has a strong proinflammatory function, such as increased angiogenesis and vasopermeability, in addition to its role in nociception. The increased number of sensory nerves seen as sprouting free nerve endings in the painful tendons may, at least partly, explain the pain. The fact that the increased number of SP fibers was not seen around blood vessels was somewhat surprising, since one might have expected a strong connection, similar to that seen in healing tendons. Instead, the existence of free nerve endings indicated that the main function of SP in tendinopathy is nociceptive rather than vasoactive.

The reduction in TH, vascular noradrenaline, suggests a role in pain modulation. Noradrenaline as a peripheral and vascular pain modulator is a topic of ongoing research. Notably, a similar pattern of decreased vascular TH and increased free SP positive nerve fibers is seen in patients with painful rheumatoid arthritis (Straub et al. 2002).

The mean VISA score of 42 combined with a mean symptom duration of three years and histopathological findings characteristic of severe tendinosis mean that the patient group is characterized by chronic and severe complaints of patellar tendinopathy.

Variation between biopsies was high, and the semi-quantitative analysis confirmed only one of the three subjective analyses of the neuromediators in question. However, the trends all pointed in the same direction. The semi-quantitative method only takes the fields with highest density of immunofluorescence into account, thus overlooking histological differences, such as extensive nerve sprouting. The semi-quantitive analysis should therefore only be regarded as a complement to the subjective analysis.

In conclusion, the results demonstrate a differentiation in the sensory and sympathetic neuromediator pattern in painful tendinopathic tendons. The dominance of nonvascular SP nerve endings, as well as the decrease of the anti-nociceptive modulator, noradrenaline, suggests a pathophysiological regulation of pain. These neuropeptides, known to be essential for normal healing, exhibit a disturbed balance that may contribute to the degenerative processes of tendinopathy.

Apoptosis

Results

Clinical characteristics. The mean age was 30 years (24-34 years, n=23) in the patient group and 29 years (19-43 years, n=11) in the control group. In the patient group, the mean number of years participating in organized training was 17 (10-28 yrs, n=23), and the mean number of total training hours per week was 14 (6-24 h, n=23). The mean VISA score was 42 (15-65, n=23), and the mean duration of symptoms was 36 months (5-120 months, n=23).

Light microscopic appearance. Biopsies from patients with a clinical history of tendon pain consistently revealed tendinosis, including areas of hypocellularity, as well as neovascularization with intimal hyperplasia, and collagen disarray and degeneration. Increased amounts of

glycosaminoglycan were localized to areas of fibrocartilagenous metaplasia or to the neointima of the vessel. Inflammatory cells were virtually absent.

Apoptosis in normal and overused tendons. Apoptotic tenocytes were identified using all three methods (F7-26, propidium iodide, caspase-3) both in normal and pathological tendon, and each method showed that apoptosis represented a small minority of total cell counts (< 1%). Apoptosis was predominantly found in fibroblast-like cells in the tendon proper. Clusters of 5 to 10 apoptotic cells were observed in the tendinosis samples, compared to scattered or no cells in the controls.

The number of apoptotic cells per unit area (4.5 mm^2) was 0.91 ± 0.81 in tendinosis samples and 0.21 ± 0.21 in controls (p=0.026). There were more areas with apoptotic cells in the tendinosis tissue (3.7 ± 0.20 vs 1.9 ± 1.2, p=0.006). In addition, fields from tendinosis patients that displayed positive staining had more apoptotic cells than positive fields from controls (3.1 ± 2.2 vs 1.5 ± 0.89, p=0.006). Although the tendinosis samples displayed increased numbers of fibroblastic cells (52 ± 32 nuclei/mm^2 vs 31 ± 16 nuclei/mm^2, p=0.021), the apoptotic index was higher (0.42 ± 0.38 % vs 0.17 ± 0.16 %, p =0.014).

Discussion

The results showed a significantly higher number of apoptotic cells per unit area and a significantly higher apoptotic index in biopsies from the patellar tendons in patients with patellar tendinopathy compared with controls. The caspases are members of a family of cysteine proteases with a sequential activation and amplification system eventually causing apoptosis (Salvesen 2002). Since caspase-3 is one of the terminal proteins in the caspase activation system (Boatright and Salvesen 2003), this finding denotes an increased apoptotic activity in the patellar tendon in patients with patellar tendinopathy compared with controls.

The caspases are synthesized as inactive zymogens and it is essential that the caspases remain inactive until the apoptotic signal is received (Boatright and Salvesen 2003). Apoptosis is typically triggered by a variety of cellular stresses including ischemia-reperfusion and oxidative stress, loss of extracellular matrix contact, excessive cytosolic calcium, cytoskeletal disruption, mechanical trauma, and others. Alternatively, disappearance of excessive fibroblasts during tissue remodelling is a normal, physiological response (Grinnell et al. 1999). In tendinopathy, the mechanisms underlying apoptosis and caspase-3 activation, and whether or not it represents a pathological or a physiological process, are not currently known. How early in the pathogenesis of tendinosis apoptosis arises remains an important question.

The link between mechanical loading conditions and the pathophysiological response in tendinopathy is obscure, and currently there is insufficient evidence to provide a direct explanation for the possible connection between the loading pattern and the in vivo pathological response (Scott et al. 2005). Paper III and Paper IV show that volleyball players with jumper's knee have better jumping ability and power generation than players who do not report symptoms from their tendons, presumably because they subject their knee extensors to higher loads when jumping and landing. Also, prevalence is higher in sports that require frequent jumping as shown in Paper I, and among athletes who train more (Ferretti et al.1984). Thus, there is reason to believe that there is a connection between the tendon loading pattern and the pathology within the tendon substance. In a study by Yuan et al. (2002), excessive apoptosis was observed at the edge of torn rotator cuff tendons in elderly patients compared with controls. This has led to the proposal that tendinosis may begin as a degenerative process involving tenocyte death (Yuan et al. 2003). In support of this model, Skutek et al. (2003) suggested that mechanical stretching of tendon fibroblasts activates cell signaling pathways leading to apoptosis. However, once ruptured the supraspinatus tendon would likely not receive excessive tensile loads, therefore other mechanisms such as oxidative stress, hypoxia, or remodelling may predominate in later stages. In another study, Barkhausen et al. (2003) found that different repetitive cyclic longitudinal stress patterns resulted in different cellular reactions dependent on the strength of the applied stress. Repetitive stress applied during one day stimulated both proliferation and apoptosis (Barkhausen et al. 2003). Our data show the number of tenocytes was increased overall, but there were also discrete areas of apoptosis and hypocellularity, suggesting that death and proliferation may be occurring simultaneously in response to repetitive loading, similar to the finding by Barkhausen et al. (2003).

One of the consistent histological findings in biopsies in tendons from patients with patellar tendinopathy is the scarcity of inflammatory cells (Karlsson et al. 1991, Khan et al. 2000a, Martens et al. 1982). In a study by Alfredsson et al. (2003), cDNA arrays and real-time quantitative polymerase chain reaction technique were used to study tendinosis and control tissue samples. Several cytokines and cytokine receptors were not upregulated, suggesting the absence of an extrinsic inflammatory process in chronic painful Achilles tendinosis.

If the primary pathology were a partial rupture, one might have expected the presence of an inflammatory response since this is the case with acute, total tendon ruptures. However, in time cellular inflammation would be expected to diminish and evolve into a typical post-inflammatory reparative response as seen in tendons and other connective tissues (increased

glycosaminoglycans and collagen synthesis, neovascularisation, hypercellularity and apoptosis of fibroblasts). In keeping with this picture, the extent of cell death observed in the current study would not be expected to trigger an inflammatory response, particularly given the poor vascularisation of tendons.

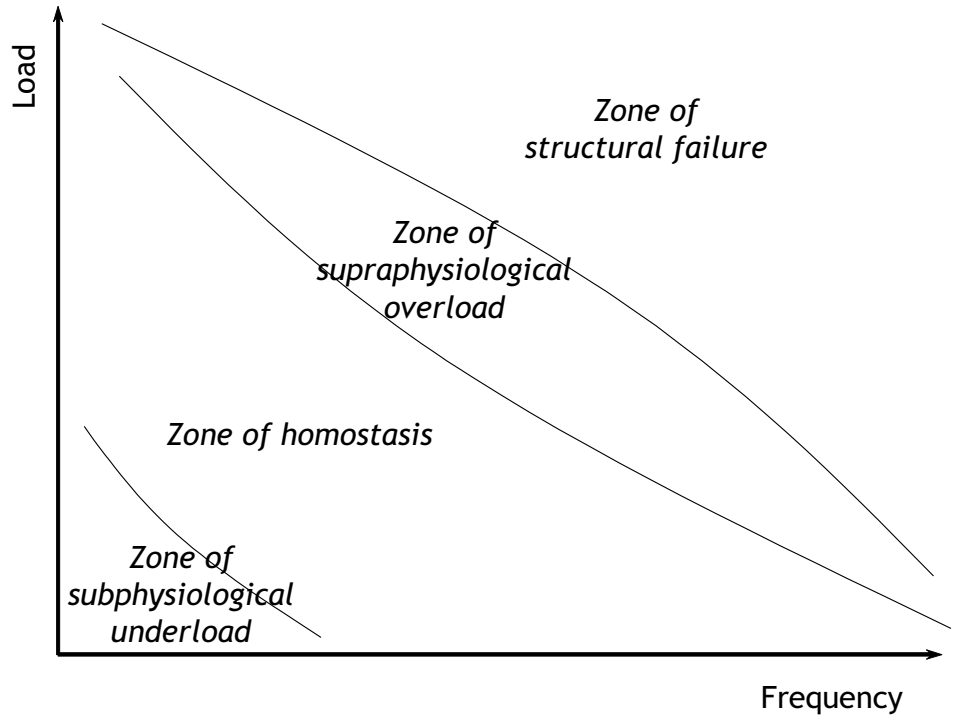
This study contributes a novel insight toward understanding the pathology of tendinosis, namely, that there is evidence of increased apoptosis in association with degenerate, non-ruptured tendon compared to controls. However, there remain several limitations that must temper conclusions. Firstly, our cross-sectional study sheds no light on whether apoptosis preceded or followed the development of tendinosis. Secondly, our data were obtained in young sports people with chronic patellar tendinosis – we may not extend our conclusions beyond this population as yet.

A model for the causation of patellar tendinopathy

Tissue homeostasis model

Dye (2005) has presented a model on the pathophysiology of patellofemoral pain. In this model he states that certain high loading conditions may induce loss of tissue homeostasis by exceeding the safe load acceptance capacity of the tissue, leading to symptomatic damage.

Figure 6. This figure describes the relationship between structural adaptation and the frequency and loading of a joint. The figure is reproduced from Dye (2005).



In this model, Dye (2005) describes a zone of load acceptance called "zone of homeostasis". By increasing the load and frequency beyond this limit the tissue will enter a zone of physiological overload, where there is gradual adaptation of tissue properties to the increased load. However, if even greater load and/or frequency is applied, structural damage will occur. The zone between subphysiological underload and supraphysiological overload is termed "the envelope of function".

Dye's model for patellofemoral pain assumes that the main causative factors are load and frequency. This seems to be the case for patellar tendinopathy, as well. Early epidemiological studies on volleyball players have shown that training frequency correlates positively with the

prevalence of patellar tendinopathy (Ferretti et al. 1984, Ferretti 1986). Moreover, sports characterized by high demands on speed and power have a higher prevalence of patellar tendinopathy (Paper I). When groups of athletes from the same sports and teams were compared, differences in total or jump training volume could be detected between asymptomatic and symptomatic athletes, at least in some cases (Paper I). However, in Paper II we found no difference between groups in the total amount of specific volleyball training. It also follows from the results that there are asymptomatic athletes who report very high training volumes and symptomatic athletes who train much less. Thus, the model above does not fully explain why some athletes develop tendinopathy and other athletes from the same team do not, despite being exposed to the same training load and frequency. Other factors must also play a significant role, either alone or by modifying tendon load or load tolerance.

Risk factor model

In order to account for interactions between different internal and external risk factors, as well as to relate these to the mechanisms by which the injuries occur, a dynamic multicausal model has been developed (Meeuwisse 1994, Bahr and Holme 2003, Bahr and Krosshaug 2005). However, this model has mainly been applied to describe the etiology of injuries with a sudden onset, resulting from a specific, identifiable event. Clinical experience suggests that such an acute trauma rarely can be recalled in cases of patellar tendinopathy, but that symptoms develop gradually over weeks and months. Thus, when applying the Meeuwisse model to explain the etiology of overuse injuries, some modifications are necessary. Mainly, this relates to the description of the injury mechanisms, the final link in the chain of leading to injury. In the case of overuse injuries, the injury mechanism is represented by the training and competition program the athlete has followed during the period the injury has developed, keeping in mind that pathology may even develop within the tissue long before symptoms occur. Thus, factors which describe the tendon loading conditions during this period, such as training volume, training frequency and type, changes in the training program, type of sport, need to be characterized to describe the injury mechanisms for overuse injuries. Different intrinsic and extrinsic factors can affect load and load tolerance, and these interactions must therefore be accounted for.

Based on the available evidence, the causes of patellar tendinopathy can be summarized as shown in Figure 7.

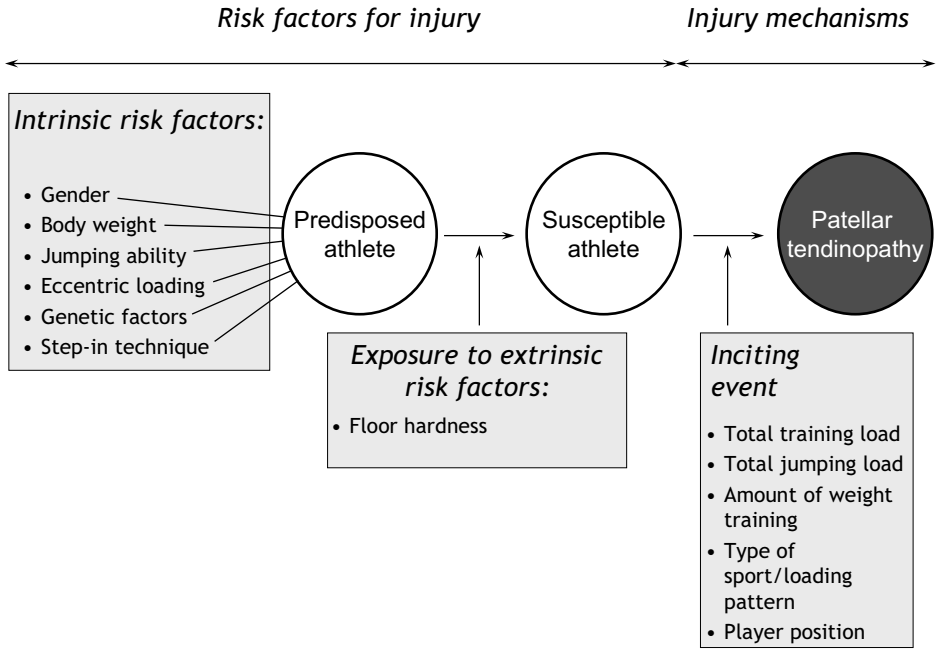


Figure 7. A dynamic, multifactorial model of the etiology of patellar tendinopathy.

Male gender is an intrinsic risk factor, because the prevalence of current jumper's knee in female handball and female soccer was 2.4 times lower compared with the corresponding male sports (Paper I). Body weight appears to be an intrinsic risk factor, because athletes diagnosed with jumper's knee weighted significantly more compared with asymptomatic athletes (Paper I and IV). In the biomechanical studies (Paper III and VI), players with jumper's knee performed better in standardized series of jump and power tests compared with the control groups. In Paper IV we found a correlation between the takeoff technique and jumper's knee. The right knee was affected twice as often as the left knee. The majority of the players used a right-left step-close takeoff technique, and none of the players reportedly preferred the right leg when landing after the attack. In fact, 20 of the 22 players with current jumper's knee on the right side used a right-left takeoff technique. This means that the leg doing the eccentric work is mostly affected. This finding may be related to the observations in Paper III, where the patient group appeared to be more effective in counter-movement jumps compared with the controls. Better eccentric performance during the decelerating part of the step-in will result in a better jumping ability, and consequently, higher tendon load when jumping.

Genetic factors are probably also of importance as shown by Mokone et al. (2006), who found that individuals with an A2 allele of the α1 type V collagen gene (COL5A1) were less likely to develop symptoms of chronic Achilles tendinopathy. However, the authors state that this

association does not prove a causal relationship, since there may be other closely linked genes involved (Mokone et al. 2006). Age was not a significant risk factor for jumper's knee in any of the present studies.

Ferretti et al. (1984) suggested a positive correlation between the hardness of the floor and the prevalence of jumper's knee among volleyball players. In line with this, it has recently been shown that the prevalence of jumper's knee among elite beach volleyball players playing on sand is only 9%, considerably lower than for indoor volleyball players (Bahr and Reeser 2003). Thus, the hardness of the floor can be regarded as an extrinsic risk factor for jumper's knee. Other suggested risk factors for jumper's knee have not been well documented yet.

Inciting event

In chronic overload injuries there is not a well defined inciting event. However, Paper I shows a small, but significantly higher training volume in players with symptoms of jumper's knee compared to asymptomatic controls. Volleyball players with jumper's knee reportedly also trained more with weights (Paper I and IV). The overall prevalence of current and previous jumper's knee was significant higher in sports characterized by ballistic movements, speed and power (Paper I). A combination of all these factors may—in an athlete predisposed by intrinsic and extrinsic risk factors—result in structural tendon damage. Thus, the loading characteristics determined by the training and competition program may be regarded as the inciting event in jumper's knee.

In the model described above, internal and external risk factors act together to make the individual susceptible to tendinopathy. For example, a volleyball player with a specific jumping technique will need to perform a certain amount of specific training on a specific floor hardness to develop tendinopathy. In our experience, the first symptoms of jumper's knee often occur after a period with increased training loads in a young athlete who is selected to a team or a training camp at a higher level of play. These talented young athletes may, from one week to the next, move from a relatively "safe" training environment—for example, practice two to three days a week, no weight lifting—to an elite club or sports school that practices daily, including intensive weight and jump training. Talented athletes are also likely to possess superior jumping ability which, when coupled with sudden increases in strength, muscle mass, and training load, further amplifies their risk of developing tendinopathy. In this setting the increased training load may be regarded as the inciting event, bringing the tendon tissue out of the envelope of function, ending up with structural damage.

Mechanotransduction

However, the link between loading conditions and structural damage is obscure. Koskinen et al. (2004) have shown that physical activity can influence the activity of local matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) in vivo, and suggest that this may be of importance in extracellular adaptation to exercise in tendon tissue. In a study by Miller et al. (2005), they found an increased synthesis of collagen in the patellar tendon after a single acute bout of strenuous, non-damaging exercise. They hypothesize that this increased collagen production may be due to some common signalling pathway transducing the mechanical stimuli into anabolic events (Miller et al. 2005). Langberg et al. (2006) showed that patients with Achilles tendinosis treated with 12 weeks of eccentric training increased their collagen synthesis rate, but the collagen metabolism in healthy controls was not affected by eccentric training. They suggest that this might indicate an inadequate adaptation of tissue strength to the activity level in tendinosis, with a subsequent tissue injury (Langberg et al. 2006). Olesen et al. (2006) have shown that loading of the plantaris tendon in rats resulted in upregulation of IGF-1 and procollagen. They suggest that the IGF-1 system probably is involved in regulation of the collagen synthesis in tendon in response to mechanical loading (Olesen et al. 2005). Lavagnino et al. (2005) have shown that tendon cells could establish an internal cytoskeletal tension through interactions with the extrecellular environment. Alterations in this tension could control the expression of both catabolic and anabolic genes (Lavagnino et al. 2005). Studies on isolated tendon cells in vitro have shown that stress deprivation results in up-regulation of interstitial collagenase, while application of a tensile load inhibits mRNA expression of interstitial collagenase, probably through the same cytoskeletally based mechanotransduction mechanism (Arnoczky et al. 2002). In a study by Mokone et al. (2005), they found that persons with variants of the tenacin-C gene with 12 and 14 guanine-thymidine repeats appeared to have a 6-fold risk of developing Achilles tendon injuries. Since mechanical signals can alter the synthesis of tenacin-C (Chiquet 1999), and tenacin-C can regulate cell-matrix interactions, the author speculate if this protein may be of importance in a possible apoptotic model of tendinopathy (Mokone et al. 2005). Arnoczky et al. (2002) have also shown, at the cellular level, that cyclic strain induces activation of stress-activated protein kinases (SAPK), possibly by a calcium-dependent mechanotransduction pathway. Since SAPK activation are important upstream regulators of the apoptosis cascade in different cell lines, they speculate if this mechanotransduction pathway may induce apoptosis and be part of the etiology in tendon overload injuries (Arnoczky et al. 2002). Scott et al. (2005) have shown that high-strain mechanical loading rapidly induced tendon apoptosis in an ex vivo rat tibialis anterior model. In Paper VI, we found excessive apoptosis in tendon biopsies from patients with patellar

tendinopathy compared with controls. This means that both at the molecular, cellular and isolated muscle-tendon level, as well as in vivo, there is reason to suggest a connection between biomechanical factors and specific anabolic and catabolic biologic responses, among them excessive apoptosis, through a mechanotransduction pathway.

In conclusion, the present model connects the loading pattern and specific extrinsic and intrinsic factors which can modify load or load tolerance to specific histopathological findings through a mechanotransduction pathway, ending up with structural damage and pain. The different anabolic and catabolic processes may be specific to the different loading conditions, initially probably in a reversible way. Understanding these relationships may be key factors to establish effective preventive measures.

Conclusions

Based on the results of the papers presented in this thesis, the conclusions are as follows:

1. The overall prevalence of current and previous jumper's knee was significantly higher in sports characterized by ballistic movements, speed and power. The condition is in most cases chronic, and athletes report significant symptoms and disability, particularly related to sport.

2. The prevalence of current jumper's knee among males was 2.4 times higher than females in comparable sports.

3. Athletes diagnosed with jumper's knee weighted significantly more compared with asymptomatic athletes, while age was not identified as a significant risk factor for jumper's knee.

4. Training volume was somewhat higher in players with symptoms of jumper's knee than controls. Also, players with jumper's knee reportedly trained more with weights.

5. Players with jumper's knee performed better in standardized series of jump and power tests compared with controls.

6. The prevalence of ultrasound changes in the patellar tendon was high among elite volleyball players, approximately 50%, but the correlation between symptoms and ultrasound changes was low.

7. Nerve fibers expressing sensory (SP) and sympathetic neuromediators (TH) appear to differ between patients with painful patellar tendinopathy and healthy controls. An increased number of SP-positive non-vascular nerve endings and a vascularly related decrease in TH were seen in patients.

8. Biopsies from the patellar tendons in patients with patellar tendinopathy displayed evidence of increased apoptosis than healthy controls.

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Paper I

Prevalence of Jumper's Knee Among Elite Athletes From Different Sports

A Cross-sectional Study

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Background: The prevalence of jumper's knee across different sports has not been examined, and it is not known if there is a gender difference. Data from surgical case series indicate that there may be a high prevalence in sports with high speed and power demands.

Hypothesis: The aim of this study was to estimate the prevalence of jumper's knee in different sports among female and male athletes and to correlate the prevalence to the loading characteristics of the extensor mechanism in these sports.

Study Design: Cross-sectional study; Level of evidence, 4.

Methods: The authors examined approximately 50 Norwegian male and female athletes at the national elite level from each of the following 9 sports: athletics (male athletes: high jump, 100- and 200-m sprint), basketball (male athletes), ice hockey (male athletes), volleyball (male athletes), orienteering (male athletes), road cycling (male athletes), soccer (male and female athletes), team handball (male and female athletes), and wrestling (male athletes). The examination included an interview on individual characteristics (weight, age, height, and training background), a clinical examination, and self-recorded Victorian Institute of Sport Assessment score from 0 (worst) to 100 (best).

Results: The overall prevalence of current jumper's knee was 14.2% (87 of 613 athletes), with a significant difference between sports with different performance characteristics (range, 0%-45%). In addition, 51 athletes (8%) reported previous symptoms. The prevalence of current symptoms was highest in volleyball (44.6% ± 6.6%) and basketball (31.9% ± 6.8%), whereas there were no cases in cycling or orienteering. The prevalence of current jumper's knee was lower among women (5.6% ± 2.2%) compared with men (13.5% ± 3.0%; χ^2 test, $P = .042$). The duration of symptoms among athletes with current jumper's knee (n = 87) was 32 ± 25 (standard deviation) months, with a Victorian Institute of Sport Assessment score of 64 ± 19.

Conclusion: The prevalence of jumper's knee is high in sports characterized by high demands on speed and power for the leg extensors. The symptoms are often serious, resulting in long-standing impairment of athletic performance.

Keywords: knee injuries; epidemiology; risk factors; patellar tendinopathy

The prevalence of jumper's knee in different sports is mostly unknown. However, among male volleyball players at the elite level, the prevalence is 40% to 50%.[13,14,24] Publications from studies on the outcome after surgery suggest that the prevalence is high in sports with high demands on speed and power, such as volleyball, soccer, and athletics.[17,27,31] As sports physicians, it seems that we see an increasing number of athletes affected by this condition, as well as more serious and long-standing complaints among those athletes diagnosed with jumper's knee. Many athletes have to reduce their training and competition levels for long periods of time, which impairs their performance levels. Despite the currently available treatment options,[5,11,26] some athletes are affected to such a degree that they have to quit sports activities. In this way, jumper's knee may seriously impair an athletic career.

The aim of the present study was to estimate the prevalence of jumper's knee in different sports and to correlate the prevalence to the sport-specific performance characteristics of these sports.[24,25] Some of the sports included were selected based on data from surgical case series,[17,27,31]

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whereas others were selected to represent sports that were thought to typify different performance characteristics. Moreover, because the prevalence among female athletes is unknown, we wanted to examine if there is a gender difference in the risk for jumper's knee. We chose to include athletes from female team handball and soccer because these are the female team sports in Norway in which the training loads are highest and so are comparable to those of male athletes in the same sports. In addition, soccer and team handball are sports characterized by high loads on the extensor mechanism, which is thought to make the athletes susceptible to jumper's knee.

METHOD

Study Design

This investigation was designed as a cross-sectional study among Norwegian athletes at the national elite level from different sports. Male athletes from 9 different sports were examined: athletics (high jump, 100- and 200-m sprint), basketball, ice hockey, orienteering, road cycling, soccer, team handball, volleyball, and wrestling. In addition, female athletes from 2 of the same sports were examined: team handball and soccer. We wanted to examine approximately 50 athletes in each sport, to provide a precision of 2% to 7% (proportion SE) for the prevalence estimate in each group. In the team sports (basketball, ice hockey, team handball, volleyball, and soccer), teams from the largest cities were invited to take part in the investigation, and all invited teams agreed to take part. The teams were examined toward the end of their competitive seasons. In the individual sports (athletics, orienteering, road cycling, wrestling), we asked athletes participating in the national championships, which were organized during the peak competition seasons, to take part in the study. All athletes who were present when we visited their teams and all athletes we approached in the individual sports agreed to take part in the study. The study was approved by the regional committee for research ethics, participation was voluntary, and consent was obtained.

Interview and Clinical Examination

Each athlete went through a standardized interview, and the information requested from each athlete included age, height, weight, and number of years participating in organized athletic training. In the team sports, we registered the number of years of participation in the top 2 divisions of the Norwegian league systems; in the individual sports, we registered the number of years of participation at the national championship level. All athletes were asked to report the number of training hours per week during the competition season (sport-specific training, weight training, jump training, and other types of training).

All athletes were also interviewed regarding present and former knee injuries and complaints. Those with current knee complaints compatible with jumper's knee went through a standard knee examination, which was conducted by 8 different sports medicine specialists. The following diagnostic criteria for jumper's knee were used: history of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with athletic activity, and distinct palpation tenderness corresponding to the painful area.[3] The diagnosis was based on a typical history and clinical findings alone because imaging techniques such as MRI and ultrasonography have shown low specificity, sensitivity, and positive predictive value in diagnosing jumper's knee.[7,9,19,24] Previous jumper's knee was diagnosed based on history alone. To assess the severity of the condition, the athletes diagnosed with current jumper's knee also self-recorded their Victorian Institute of Sport Assessment (VISA) scores.[34] This is a validated pain and function index with a high score of 100 (no symptoms) and low score of 0 (maximum symptoms) that has been developed specifically for this purpose and has been shown to be a valid measure of symptoms.[32]

Data Analysis

For continuous variables, the results are given as means ± SD, unless otherwise noted. Proportions are reported with the corresponding SE, where relevant. Prevalence was compared between groups using Pearson chi-square tests. Multiple logistic regression analysis was used to test the effect of potential risk factors for patellar tendinopathy (age, height, weight, experience at the elite level, and volume of sport-specific training, weight training, and jump training), adjusting for differences between sports. Comparisons of continuous data between groups were done using analysis of variance (ANOVA) or unpaired *t* tests, as noted in the Results. An alpha level of .05 was considered significant.

RESULTS

The overall prevalence of current jumper's knee was 14.2% ± 1.4% (87 of 613 athletes). Of the 87 athletes with current symptoms, 37 had bilateral symptoms, whereas 30 athletes had symptoms from the right side only, and 20 athletes had symptoms from the left side only. This finding means that the prevalence of current jumper's knee affecting the right knee was 10.9% (67 players) and affecting the left knee was 9.3% (57 players). In addition, 51 athletes (8.3%) reported previous symptoms of jumper's knee affecting one or both legs, resulting in a prevalence of current or previous symptoms of 22.5% (138 of 613 athletes). Only 1 athlete with a diagnosis of current jumper's knee localized the pain to the quadriceps tendon insertion at the upper patellar pole, and the rest localized the pain to the patellar tendon.

As shown in Figure 1, there were significant differences in the prevalence of current jumper's knee (χ^2 test, $P < .001$), as well as in the prevalence of previous symptoms (χ^2 test, $P < .001$). The prevalence of current symptoms was highest in volleyball with 44.6% ± 6.6% and in basketball with 31.9% ± 6.8%, whereas there were no cases in cycling or orienteering. Also, the prevalence of current jumper's

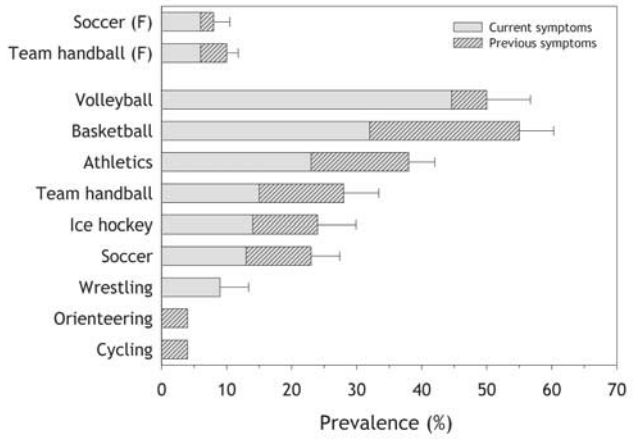

Figure 1. Prevalence (%) of current (gray bars) and previous (hatched bars) symptoms of jumper's knee. The results for female athletes (F) are shown in the 2 upper bars; the rest of the results are for male athletes. Error bars denote SE.

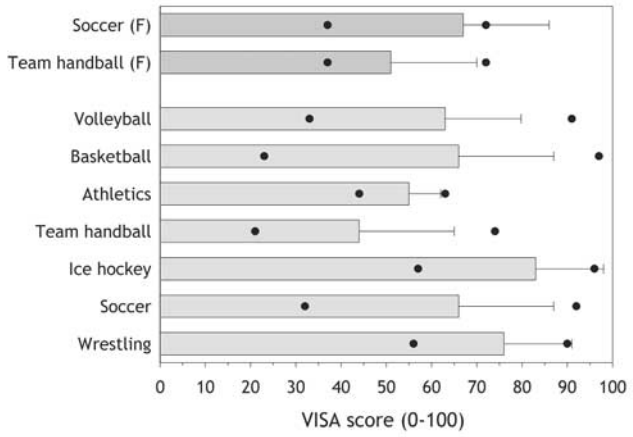

Figure 2. The Victorian Institute of Sport Assessment (VISA) scores for players with current symptoms of jumper's knee in the various sports groups. For players with bilateral symptoms, the lowest value (worst knee) has been used. The top 2 hatched bars show the results for female athletes (F) from soccer and team handball; the gray bars show the results for male athletes. No results are given for orienteering and cycling because there were no athletes with current symptoms in these groups. The bars and error bars denote the mean and SD. In addition, the filled circles show the lowest and highest values in each group.

knee was lower among women, with 5.6% ± 2.2% (6 of 107 team handball and soccer players) compared with a combined prevalence of 13.5% ± 3.0% (18 of 133) in the corresponding male sports (χ^2 test, $P = .042$).

The mean symptom duration among athletes with current jumper's knee was 32 ± 25 months (range, 1-144 months; n = 87). There was a significant difference in symptom duration between the 9 different sports (analysis of variance, $P = .04$). Moreover, there was no difference (t test, $P = .48$) in the duration of symptoms between female (22 ± 12 months; n = 6) and male athletes (28 ± 21 months; n = 55).

The mean VISA score reported across sports and genders was 64 ± 19. As seen in Figure 2, the VISA score reported by players with current symptoms of jumper's knee was significantly different between sports (ANOVA, $P = .003$). The lowest VISA score was reported by male team handball players and the highest by ice hockey players. However, there was no gender difference. The VISA score in female team handball and soccer was 59 ± 15, compared with 58 ± 23 in the same male sports (ANOVA, $P = .9$).

The number of years of participation in organized training was 15.2 ± 5.1, with 6.1 ± 4.2 years at the elite level (Table 1). The number of hours with sport-specific training was 11.8 ± 3.9 (Table 2). There was no significant difference in these variables between athletes with current jumper's knee and those without. However, athletes with current jumper's knee weighed more (83.6 ± 11.6 kg vs 77.3 ± 11.9 kg; $P < .001$), were taller (186 ± 9.5 cm vs 181 ± 9.2 cm; $P < .001$), and did significantly more weight training (3.5 ± 2.4 h/wk vs 2.5 ± 2.1 h/wk; $P < .001$) and jump training (1.1 ± 1.8 h/wk vs 0.5 ± 1.0 h/wk; $P < .001$).

The comparison between athletes with current jumper's knee and those without in each specific sport showed that in basketball, the athletes with jumper's knee did significantly more sport-specific training than did those without jumper's knee (14.7 ± 2.7 h/wk vs 12.3 ± 2.5 h/wk; $P = .005$). In male handball, the athletes with jumper's knee did significantly more plyometric training compared with those without jumper's knee (0.7 ± 1.0 h/wk vs 0.2 ± 0.3 h/wk; $P = .01$). In male soccer, the jumper's knee group was significant taller than were the others (186 ± 4.3 cm vs 183 ± 5.5 cm; $P = .05$). Otherwise, there were no other significant differences between those with jumper's knee compared to those without in the other variables outlined in Tables 1 and 2. In a logistic regression model that included gender, sport, age, height, weight, training background, and the volume of the different types of training, only weight training and jump training were significant factors.

DISCUSSION

The main finding of this study was that the overall prevalence of jumper's knee was 14% across the sports included. In addition, 8% of the athletes reported previous symptoms, indicating that every fifth elite athlete is affected by jumper's knee during his or her athletic career. The prevalence varied between sports—from no cases in cycling and orienteering to 45% with current symptoms in male volleyball. It should also be noted that the mean duration of the symptoms was 32 months, with a mean VISA score of 64. The information on the duration of the symptoms was based on memory, which means that the precision of this information is uncertain. Nevertheless, it seems clear that even with this limitation, there is no doubt that the majority of patients have played with symptoms for several years. The VISA score is a validated method to describe the seriousness of symptoms in tendinopathy.[32,34] This

TABLE 1
Athlete Characteristics[a]

	n	Age, y	Height, cm	Weight, kg	Organized Training, y	Elite Level, y
Male athletes						
Bicycling	50	24.7 ± 5.1	182 ± 7.6	72.0 ± 6.2	13.5 ± 6.3	6.4 ± 4.2
Orienteering	52	22.1 ± 5.3	182 ± 5.6	71.3 ± 7.4	12.4 ± 4.6	5.4 ± 3.1
Wrestling	43	24.2 ± 5.9	174 ± 9.5	75.8 ± 12.0	15.5 ± 5.8	7.8 ± 6.1
Ice hockey	51	25.0 ± 4.1	182 ± 5.1	85.1 ± 7.0	17.6 ± 4.5	7.9 ± 4.2
Athletics	48	25.1 ± 4.7	185 ± 8.2	78.3 ± 8.0	12.5 ± 4.7	6.1 ± 3.9
Basketball	47	24.1 ± 5.1	191 ± 8.6	87.3 ± 10.5	12.4 ± 5.6	4.9 ± 4.8
Soccer	85	25.6 ± 4.1	183 ± 5.5	79.5 ± 11.4	18.3 ± 4.1	6.7 ± 3.8
Team handball	48	23.6 ± 3.8	187 ± 6.2	89.6 ± 10.4	14.6 ± 4.9	5.0 ± 3.9
Volleyball	56	26.8 ± 4.2	192 ± 6.0	88.8 ± 7.2	16.7 ± 4.7	7.2 ± 4.0
Female athletes						
Soccer	55	23.1 ± 3.3	169 ± 4.8	63.2 ± 5.1	15.7 ± 3.2	4.7 ± 2.9
Team handball	52	22.8 ± 4.3	172 ± 6.0	68.8 ± 8.4	14.9 ± 4.2	4.7 ± 4.6

[a]Values are presented as means ± SD.

TABLE 2
Training Volumes Reported by the Different Groups of Athletes[a]

	Sport-Specific Training, h/wk	Weight Training, h/wk	Jump Training, h/wk	Other Types of Training, h/wk
Male athletes				
Bicycling	17.9 ± 4.0	2.8 ± 1.4	0.0 ± 0.0	4.5 ± 4.8
Orienteering	10.8 ± 3.6	2.7 ± 1.1	1.2 ± 0.7	2.6 ± 1.6
Wrestling	8.6 ± 2.9	5.0 ± 2.7	0.0 ± 0.3	1.0 ± 1.8
Ice hockey	13.0 ± 3.2	2.7 ± 1.1	1.0 ± 0.1	2.6 ± 1.6
Athletics	9.0 ± 3.5	4.5 ± 2.1	3.0 ± 2.3	0.9 ± 1.8
Basketball	13.0 ± 2.8	5.5 ± 2.3	0.9 ± 1.4	0.4 ± 1.1
Soccer	13.0 ± 3.9	2.5 ± 0.5	0.7 ± 0.4	1.3 ± 1.3
Team handball	10.7 ± 2.4	3.5 ± 1.7	0.3 ± 0.5	0.8 ± 1.1
Volleyball	10.4 ± 2.4	2.1 ± 1.9	0.6 ± 0.9	0.2 ± 1.3
Female athletes				
Soccer	10.6 ± 2.1	2.0 ± 1.5	1.0 ± 0.6	1.7 ± 0.9
Team handball	11.4 ± 3.1	2.6 ± 0.9	1.0 ± 0.6	2.2 ± 1.5

[a]Values are presented as means ± SD.

means that this condition can severely interfere with athletic performance and even threaten an athletic career. Based on these data, it could be claimed that for some sports, jumper's knee may cause at least as much impairment for athletic performance as do acute knee injuries.

These prevalence figures probably represent minimum estimates. The clubs of the team sport athletes were typically visited during a training session, in which all those present were invited to be examined. Similarly, in the individual sports, we examined the athletes at their national championships. The response rate was excellent—none of the athletes declined the invitation to participate. However, the athletes with the most serious problems, those who could not participate in training or competition, were not included in the study. As an example, we know that in men's team handball, there were 4 players who had recently been treated surgically for jumper's knee among the teams included in this study. We do not know the number of athletes in the other sports who were too disabled to be included. This may be a significant source of error, particularly in the individual sports where it is more likely that athletes would withdraw or not even enter the national championships if they thought that they could not perform fully. Also, an unknown number of athletes may have retired early because of jumper's knee, and some may have settled for a career at a lower level of performance because they could not tolerate the heavy training and competition load at the elite level. Thus, the elite samples we were able to study represent the survivors, and the true career prevalence is higher than the 22% reported here as an overall result across the sports included.

Another methodological limitation that must be considered when interpreting the findings is that the results were based on clinical examination alone. For practical reasons, we were not able to do MR or ultrasound imaging to confirm the presence of structural tendon changes. This means that to be recorded as having current symptoms of jumper's knee, the athlete had to report a painful tendon

during athletic activity with corresponding palpation tenderness. It may be argued that this definition is unspecific because we did not know for certain that the tendon was the source of the pain in all cases. For instance, we could not rule out cases with referred pain, principally from the distal aspects of the articular surface of the patella. In fact, a number of studies have shown that the correlation between clinical findings and ultrasound[9,19,22,24,30] or MR examinations is low[4,10,18] and even that symptoms and tendon changes come and go independently.[8,9] A significant number of athletes have or develop visible tendon changes without symptoms of jumper's knee, and some have significant pain without detectable tendon changes.[8,23] Thus, we would argue that the current clinical definition provides the most valid estimate for the prevalence of jumper's knee because it will detect all players with tendon symptoms during athletic performance.

To our knowledge, there are no previous reports on the prevalence of jumper's knee across different sports. A number of case series presenting the outcome after surgical treatment indicate that the majority of patients are from sports with high demands on speed and power.[17,27,31] Raatikainen et al[31] from Finland described 182 patients who underwent surgery for jumper's knee and found that 46% were from athletics, 37% from volleyball, 5% from soccer, and the rest from other sports. On the other hand, Martens et al[27] from Belgium found that only 8% of their 90 surgically treated patients were from athletics, whereas 34% were volleyball players and 32% were soccer players. Furthermore, Karlsson et al[17] from Sweden reported that of 81 patients they treated for jumper's knee, only 9% were volleyball players, whereas 37% were from athletics and 27% were from soccer. In these 3 studies, basketball accounted for less than 10% of patients. As illustrated by the conflicting results from these[17,27,31] and other studies (for a complete review of surgical studies, see Coleman et al[5]), it is not possible to estimate prevalence from case series because the population at risk is unknown. The differences observed in the proportion of patients from different sports may simply reflect how popular these sports are in the different countries.

Previous studies reporting on the prevalence of jumper's knee in a defined cohort of players are few and mainly limited to volleyball[12,15,24] and basketball.[7,9] Ferretti[12] and Ferretti et al[15] found in their studies on volleyball players that approximately 40% had jumper's knee. Similarly, Lian et al[24] showed, based on a clinical examination of 47 male elite volleyball players, that 25 had current symptoms and an additional 7 reported previous symptoms of jumper's knee. In other words, it appears that the prevalence of jumper's knee among elite volleyball players is between 40% and 50%, and this is confirmed by the present data. Cook et al[7] examined the patellar tendons of a cohort of elite basketball players using ultrasonography. They showed that 29% of the tendons examined displayed hypoechoic sonographic regions. However, the study did not report how the tendon changes correlated with symptoms. In other sports investigated in this study, the prevalence of tendon changes was lower than in basketball (14% Australian Rules football, 7% cricket, and 6% netball). In adolescent basketball players (14-18 years old), the prevalence was similar to that of adults, with 26% having imaging changes, whereas only 7% had symptoms (11% males and 2% females).[9] In these 2 studies, 2% to 4% of the control populations studied exhibited tendon changes.[7,9]

In both of the ultrasound imaging studies, the ratio of male to female abnormalities was 2:1. However, to date, it is not known if there is a gender difference in the risk for jumper's knee, as there is for acute knee injuries, particularly ACL tears.[1,29] The present results suggest that jumper's knee is twice as common among male athletes as it is among female athletes. The prevalence of current symptoms was 5.6% among female team handball and soccer players, compared with 13.5% in the corresponding male sports. The question is, What is the cause of the apparent gender difference? We chose team handball and soccer to examine the gender difference because these are sports in Norway that are played at an equally high performance level by men and women; therefore, we thought player experience and training volumes would be similar, and we expected a high prevalence of jumper's knee. As seen from Tables 1 and 2, the training volumes (15-17 h/wk total training time) and background (15-18 years of organized training, 5-7 years at the elite level) were similar between men and women. The difference in prevalence can be attributed to a number of other factors. It is well documented that jumping ability and force-generating capacity are lower among women than men.[28] So, even if the number of sprints and jumps may be similar between men and women playing the same sports, the lower prevalence may simply reflect that the lower forces transmitted through the quadriceps and patellar tendons are lower among women.

As expected, in the present study, the prevalence was high in basketball (55% reporting current or previous jumper's knee), a sport characterized by high demands on speed and power. The maximal muscle force that can be generated eccentrically is 1.5 to 2.0 times higher than is the maximal isometric force and is several-fold higher than the maximal concentric force, especially at high speeds.[16] Also, the ground reaction force is different between different tasks, ranging from 2.8 times body weight during distance running to 6 times body weight during jumping in volleyball and 10 times body weight in a long jump takeoff.[28] The highest ground reaction forces are seen with ballistic drop jumps, and the resulting forces through the extensor tendons are proportional to the ground reaction force. Therefore, it is reasonable to suggest a connection between the loading pattern of the knee extensors and the prevalence of jumper's knee. This supposition seems to match the prevalence distribution seen in the present and previous studies, with the highest in basketball and volleyball (high jump volume and eccentric load); athletics (sprinters and jumpers, high load but less volume); team handball, soccer, and ice hockey (less jumping, some sprinting); and low prevalence among orienteerers (high volumes of running but no sprinting) and road cycling (high volumes of concentric work, no ballistic loading).

We have previously shown in a case-control study[23] and a cohort study[25] that volleyball players with jumper's knee

have better jumping ability and power generation than do players who do not report symptoms from their tendons, presumably because they subject their knee extensors to higher loads when jumping and landing. Ferretti et al[15] have shown that there is a linear relationship between training volume and prevalence of jumper's knee among volleyball players and that the harder the floor type they trained on, the higher the prevalence of jumper's knee. In line with this finding, it has recently been shown that the prevalence of jumper's knee among elite beach volleyball players was only 9%, considerably lower than in indoor volleyball players.[2] The explanation for this difference in prevalence is probably that jumping and landing in the soft sand are less demanding on the tendon than is jumping on indoor playing surfaces. In other words, there is ample evidence to suggest a link between the total load on the tendon and the prevalence of tendon injury.

However, the link between the mechanical loading conditions and the pathophysiological response is obscure. It has been suggested that mechanical overload produces partial tears in the ligament substance,[23,25] and the histologic findings have been interpreted as partial tendon ruptures.[17,27] This theory has been questioned,[20,21] and it has recently been suggested that the initial injury is to the tenocyte, not to the collagen fibers.[6,35] However, to date, there is insufficient evidence to provide a direct explanation for the apparent connection between the loading pattern and the pathologic response. Skutek et al[33] suggested that mechanical stretching of tendon fibroblasts activates signaling pathways that in the next step induce apoptosis. Tendon tissue is characterized by a homeostatic balance, as in all other living tissues, with both inhibitory and stimulating signals. The uniform histologic findings seen with tendinopathy are compatible with an apoptotic process. It may be that when the mechanical loading conditions surpass the adaptive responses of the cells, an apoptotic process is induced.

CONCLUSION

The overall prevalence of jumper's knee is 14%, with an additional 8% reporting previous symptoms, which suggests that the career prevalence is at least 22%. Jumper's knee is twice as common among male athletes as it is among female athletes. However, the prevalence varies greatly between sports—with a high prevalence in sports characterized by high-impact ballistic loading of the knee extensors and low prevalence in sports with low loads—suggesting that there is a link between the prevalence of jumper's knee and total tendon load. The high prevalence, long duration of symptoms, and low function scores suggest that in some sports, jumper's knee may be one of the main causes of impairment in athletic performance.

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Paper II

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Relationship between symptoms of jumper's knee and the ultrasound characteristics of the patellar tendon among high level male volleyball players

Lian Ø, Holen KJ, Engebretsen L, Bahr R. Relationship between symptoms of jumper's knee and the ultrasound characteristics of the patellar tendon among high level male volleyball players.
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This study assessed the ultrasound characteristics of the patellar tendon in two groups of volleyball players, one group without knee symptoms and one group with symptoms of jumper's knee. Of 47 male elite players, 25 were diagnosed to have current and seven to have had previous symptoms of jumper's knee, as determined by clinical examination. Since some players had bilateral problems, there were 34 knees with current problems and nine with previous problems. Seven of the 30 knees with a clinical diagnosis of jumper's knee in the patellar tendon had normal ultrasound findings, and ultrasound changes believed to be associated with jumper's knee (tendon thickening, echo signal changes, irregular paratenon appearance) were observed in 12 of 51 knees without symptoms. Specific ultrasound findings such as paratenon changes, hypoechoic zones or pathological tendon thickness proximally did not correlate significantly with the degree or the duration of symptoms. This study suggests that the specificity and sensitivity of ultrasonography is low in the evaluation of patients with mild symptoms of jumper's knee.

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Key words: tendon injuries; patellar tendon; ultrasonography; volleyball

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Volleyball is a sport characterized by a high number of maximal jumps. Many players suffer from patellar or quadriceps tendon pain, described as the syndrome of jumper's knee by Blazina et al. (1–3). Numerous histological (4–10) and soft tissue imaging studies (5, 8, 9, 11–16) have shown tendon abnormalities in patients with jumper's knee, sometimes explained as the consequences of a non-healed, or insufficiently healed, partial patellar tendon tear (6).

Recent studies have shown that ultrasound is highly accurate in showing tendon tears, later confirmed during surgery, in athletes with disabling patellar tendon pain (6–9, 12, 17, 18), but to our knowledge only one study has compared the clinical diagnosis of jumper's knee with ultrasound findings in players with less serious symptoms (8). The purpose of this study was to examine and compare the ultrasound characteristics of the patellar tendon in two groups of high-level volleyball players, one asymptomatic group, and one group with symptoms of jumper's knee.

Methods

Study design

The study was carried out during an international volleyball tournament in Oslo, Norway in May 1994 with approval from the Ethics Committee of The Norwegian Research Council. The tournament was played 2 months after the end of the regular league season, with teams competing in classes according to their level of play. The six Norwegian teams participating in the men's elite division in the tournament were invited to take part in the study. These were amateur teams that otherwise compete in the top division of the Norwegian Volleyball Federation leagues. The teams consisted of 53 players, and of these 47 (89%) consented to participate in an

interview, a clinical examination, and an ultrasound examination of both knees.

Interview and clinical examination

The players were asked about present and former knee injuries and complaints, specifically about symptoms of jumper's knee, in an interview with an orthopaedic surgeon. The knee examination included palpation of the patellar and quadriceps tendons, a manual isometric test of the extensor apparatus in full extension, 30° and 90° of flexion, assessing the pain response, as well as two chondromalacia tests (a patellar grinding test, and a 30-s isometric extension test with the knee in 30° of flexion). Palpation of the patellar tendon was performed with the quadriceps muscles relaxed, and the patella was pushed in a distal direction, thereby affording better access for palpation of the tendon.

The following diagnostic criteria for jumper's knee were used: history of pain from the quadriceps or patellar tendons or their patellar or tibial insertions when playing volleyball, and tenderness to palpation corresponding to the painful area (1). The diagnosis of previous jumper's knee was based on medical history alone. The patients were classified according to criteria modified from Blazina et al. and Roels et al. (Table 1) (1, 4).

Ultrasound examination

Ultrasonography was performed using a 7.5 MHz real-time, linear array probe (Model Sonoline SI 400, Siemens, Germany). A stand-off gel mattress was used to enhance the image. The players were scanned in a supine position with the knee in about 30° flexion to ensure an extended tendon (9, 19). All ultrasound examinations were performed by an experienced ultrasonographer (KH) who was blinded to the patient's history and the results of the clinical examination. The patellar tendon was examined for any of the following changes: hypo- or hyperechoic zones, signal changes in the anterior surface or the posterior margin, and bursa appearance (Fig. 1A–C). Care was taken to hold the probe perpendicular to the tendon (9, 19). The length of any hypoechoic zones was recorded. Prints of the images were also obtained for future reference.

The lengths of the patella and patellar tendon were measured using longitudinal scans (Fig. 2). Similar to the Insall–Salvati index (20), an index of patellar length to patellar tendon length was calculated. Finally, the proximal and mid-part width and thickness of the tendon were measured using transverse scans (Fig. 2). Assuming an ellipsoid shape, the proximal and midpart cross-sectional areas of the tendon were calculated as: $\pi \times (W/2) \times (T/2)$, where W is the width and T is the thickness of the tendon.

Data analysis

Results are given as means ± SD and/or range unless otherwise noted. Prevalence was compared between groups using a chi-square test. Comparisons of continuous data between groups were done using unpaired *t*-tests (two groups) or ANOVA (three or more groups). An alpha level of less than 0.05 was considered significant.

Results

Prevalence of jumper's knee

Of the 47 players participating in the study, 25 players (53±7%) fulfilled the diagnostic criteria for jumper's knee with current symptoms affecting at least one side, giving a total of 34 knees with this diagnosis, since nine of the players had bilateral problems (Table 2). An additional nine knees had had previous problems that were identified as jumper's knee, giving a total of 43 knees with current or previous symptoms (Table 2).

Of the 34 knees with current complaints of jumper's knee, the onset of symptoms was reported as gradual in 32 cases (94%) and acute in two cases.

Table 1. Classification of jumper's knee according to symptoms as outlined by Roels et al. (4) and the current classification system

	Roels et al. (4)	Current classification
Grade I	Pain at the infrapatellar or suprapatellar region after practice or after an event	Same
Grade II	Pain at the beginning of the activity, disappearing after warm-up and reappearing after completion of activity	Same
Grade III	Pain remains during and after activity and the patient is unable to participate in sports	IIIa: Pain during and after activity, but the patient is able to participate in sports at the same level
		IIIb: Pain during and after activity and the patient is unable to participate in sports at the same level
Grade IV	Complete rupture of the tendon	Same

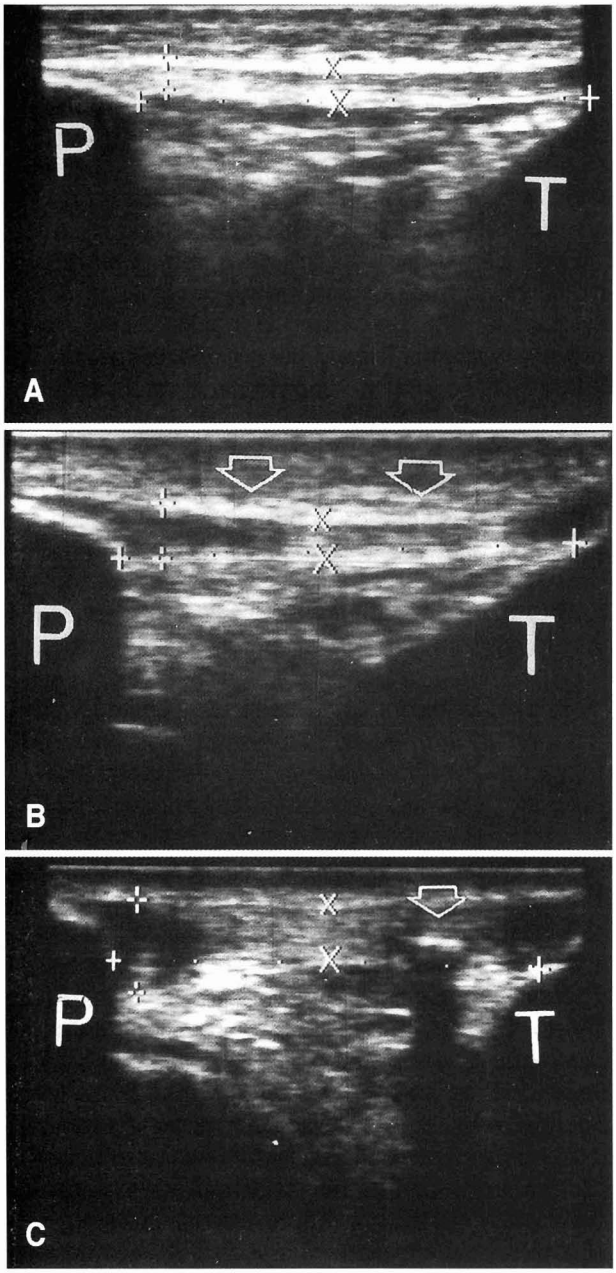

Fig. 1. (A) Ultrasonogram of a normal patellar tendon. Note the uniform thickness in the proximal and distal parts of the tendon and the homogeneous echogenicity. P denotes the distal tip of the patella, and T denotes the tibial tuberosity. The crosses denote the reference points used for the length and thickness measurements (Fig. 2). (B) The patellar tendon of a player with no previous or present history of jumper's knee. The ultrasonogram shows thickening (arrows) of the proximal part of the tendon, which also is hypoechoic. There is also thickening of the paratenon in the central part of the tendon. (C) The patellar tendon of a player with grade III symptoms (modified Blazina–Roels classification). Note thickening of the entire tendon with marked hypoechoic changes in the proximal part. Also note the the hyperechoic zone (arrow) in the distal part of the tendon (calcification after partial tear?).

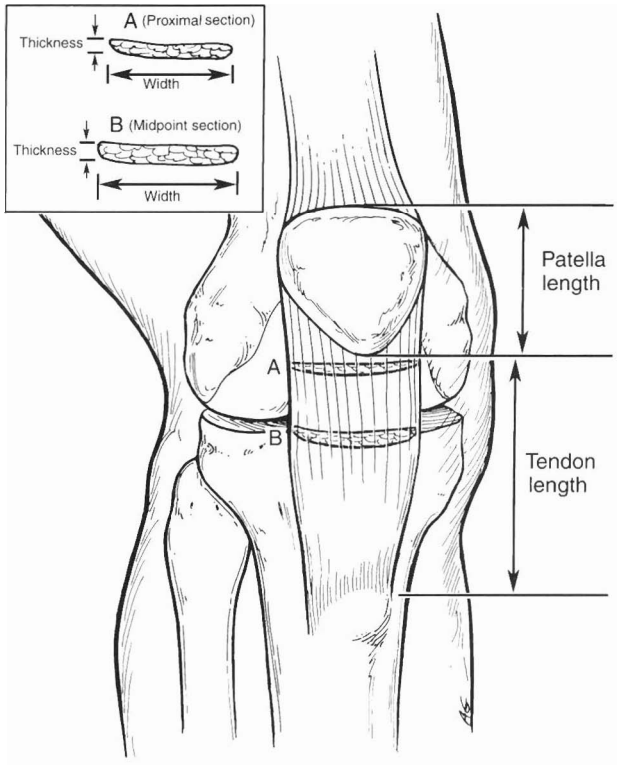

Fig. 2. Measurements of patellar length, and patellar tendon length, width and thickness as made on ultrasound scans.

The age at symptom onset was 18.8±2.8 years (13.5–25.9) and the duration of symptoms was 3.5±2.4 years (range: 0.1–10). The severity of symptoms was classified as grade I in four knees, grade II in 19 knees and grade IIIa in 11 knees (Table 1). The painful area was located in the patellar tendon in 27 cases and at the insertion of the quadriceps tendon in four cases. In three of the cases, both sites were affected.

Palpation tenderness was found in a number of players who did not complain of symptoms of jumper's knee, and the predictive value of pain on isometric contraction was low (Table 3). Previous Osgood–Schlatter's disease was reported in two cases among those with current jumper's knee (34 knees), and in eight of 60 knees without current symptoms (NS).

Table 2. Prevalence of diagnosis of current or previous jumper's knee (n = 47 players; n = 94 knees)

Side	Current jumper's knee	Previous jumper's knee	Current or previous jumper's knee
Right knee	22 (47%)	3 (6%)	25 (53%)
Left knee	*12 (26%)	6 (13%)	18 (38%)
Sum knees	34 (36%)	9 (10%)	43 (46%)

*Significant difference in prevalence between right and left knees (chi-square).

Table 3. Clinical findings in 34 knees with current jumper's knee and 51 knees without symptoms. Knees with previous symptoms (n=9) only were excluded from the analysis

Test	Test result	Current symptoms (n=34)	No symptoms (n=51)
Palpation tenderness	Negative	–	39
	Slight	9	6
	Moderate	12	6
	Strong	13	–
Pain on isometric contraction (0°)	No	24	48
	Yes	10	3
Pain on isometric contraction (30°)	No	29	51
	Yes	5	–
Pain on isometric contraction (90°)	No	31	51
	Yes	3	–
Chondromalacia tests	Negative	27	43
	Positive	7	8

Table 4. Dimensions of the patellar tendon and patella in athletes with (n=30 knees) or without (n=51) current symptoms of jumper's knee. Knees with previous symptoms or symptoms from the quadriceps tendon only were excluded from the analysis (n=13). Values are means±SD

	No symptom	Current symptoms	Significance level (P)*
Tendon length (mm)	52±5	53±7	0.29
Patella length (mm)	38±3	39±3	0.79
Insall–Salvati index	0.75±0.10	0.73±0.08	0.46
Proximal thickness (mm)	3.8±1.1	6.2±2.2	<0.001
Proximal width (mm)	33±3	33±4	0.65
Proximal area (mm)	99±29	161±60	<0.001
Midpoint thickness (mm)	3.9±0.7	4.1±0.5	0.21
Midpoint width (mm)	36±3	37±6	0.003
Midpoint area (mm^2)	108±20	120±19	0.08

*Unpaired t-test.

Tendon changes observed by ultrasonography

The anteroposterior thickness of the tendon was increased in the knees classified as having current jumper's knee compared to knees without symptoms, excluding knees with previous jumper's knee or symptoms from the quadriceps tendon only (Table 4). No other differences in tendon dimensions were noted.

The degree of clinical symptoms could not be reliably predicted from the changes observed in paratenon appearance or by the presence of hypoechoic changes (Table 5). The length of the hypoechoic zone was 1 1.5±4.2 mm among those without symptoms, and 10.0±0.0 mm, 14.4±2.8 mm and 20.1±8.4 mm among those with grade I, II and IIIa symptoms, respectively (NS, ANOVA).

No increase was observed in proximal tendon thickness or length of any echoic changes observed in relation to the duration of current symptoms of jumper's knee.

Table 5. Relationship between specific findings on ultrasonography and grading of symptoms of jumper's knee (n=81 knees). Knees with previous symptoms or symptoms from the quadriceps tendon only were excluded from the analysis (n=13)

		Clinical classification			
Ultrasound parameter	Test result	Normal (n=51)	Grade I (n=4)	Grade II (n=16)	Grade IIIa (n=10)
Paratenon changes?	No	23	–	4	2
	Yes	28	4	12	8
Hypoechoic changes?	No	40	2	3	3
	Yes	11	2	13	7

Discussion

The main findings of this study were that the prevalence of jumper's knee and ultrasound changes in the patellar tendon was high, approximately 50%, but that the correlation between symptoms and ultrasound changes was low.

In describing patients with jumper's knee, we propose a modification to Roels et al.'s (4) clinical grading system. According to Blazina et al. and Roels et al. (1, 4), there are several patients who are able to play matches and practise despite having pain throughout the activity, but for whom there is no available classification category. We therefore suggest splitting grade III into grade IIIa for patients with pain during activity, but who are still able to train and play matches, and grade IIIb for those with disabling pain (Table 1). This modification will enable a more precise patient classification in future epidemiological and clinical studies. The prevalence of jumper's knee among high level volleyball players observed in the present study was somewhat higher than that previously reported by others (3, 21, 22). However, the true proportion of affected players may be even higher, since neither this nor previous studies have included players with disabling problems (grade IIIb).

To our knowledge, the only previous study comparing the clinical and ultrasound-based diagnosis of jumper's knee is by Myllymäki et al. (8). Of 62 knees with characteristic symptoms of jumper's knee, they reported no hypoechoic changes in 31 (50%). In the present study, seven of the 30 knees with a clinical diagnosis of jumper's knee in the patellar tendon had normal ultrasound findings. On the other hand, we found ultrasound changes believed to be associated with jumper's knee (tendon thickening, echo signal changes, irregular paratenon ap-

pearance) in 12 of 51 knees without current or previous symptoms.

Despite this, several studies have shown near-perfect correlation between preoperative ultrasound changes and surgical findings (6, 7, 9, 12, 17, 18). However, as these studies were carried out in a selected patient group, i.e. almost all of them had disabling symptoms (grade IIIb) who did not respond to non-operative treatment, the results should be interpreted carefully when applied to other patient populations. Indeed, the results of the present study and that of Myllymäki et al. (8) show that the correlation between ultrasound changes and symptoms is weak among athletes with less serious symptoms. This apparent discrepancy between the presence of pain and anatomic tendon changes needs to be resolved.

Thus, in order to address this question, information is necessary on the pathophysiology of jumper's knee and corresponding ultrasound manifestations. Several authors have described the histopathological changes in the patellar tendon obtained from surgical specimens in patients with disabling jumper's knee, and their observations usually include tearing of tendon fibres, regeneration with fibroblast proliferation, myxomatous degeneration and capillary proliferation (4, 10, 17, 23, 24). These findings are interpreted as non-healed or insufficiently healed partial tears of the tendon. There is usually no or very sparse inflammatory response. Again, these observations were from patients with disabling symptoms (grade IIIb), among whom conservative treatment methods had failed. To our knowledge, there is no available information on the histopathological changes in patients with Roels' grade I, II or III disease, or the natural history of jumper's knee (25). In spite of the lack of this information, attempts have been made to correlate ultrasound changes and anatomical findings to the clinical staging of the disease (5, 11).

Jerosch & Schröder (11) suggested that a relationship exists between the severity of the pathological changes and certain ultrasound characteristics. More serious disease is assumed to be associated with wide-spread thickening of the tendon, echoic changes and surface irregularities. We found no correlation between the presence of surface changes suggesting paratenon pathology, and either the presence of symptoms or the degree or duration of symptoms. This suggests that paratenon changes do not necessarily constitute a sign of more serious clinical disease.

Karlsson et al. (26) studied 91 patients with grade III symptoms and hypoechoic changes on ultrasound examination. When the patients were grouped according to the length of the hypoechoic zones, only 6.6% of the patients with changes of <10 mm needed surgical treatment, whereas 38.5% of those with changes of >20 mm subsequently needed surgical treatment (26). This suggests that the length of the hypoechoic zone may be a significant factor in planning treatment. However, we did not find any correlation between clinical staging and the length of the hypoechoic changes, nor could we find any relationship with the duration of symptoms. Since there appears to be a correlation between the size of the hypoechoic area and the effect of non-operative treatment, but no correlation between size and clinical staging or duration of symptoms, this may be one reason why the relationship between clinical stage and effect of non-operative treatment can be difficult to predict.

When comparing normal tendons and tendons with symptoms of jumper's knee, we found a significant difference between the asymptomatic and symptomatic players in anteroposterior tendon thickness, particularly in the proximal part of the tendon, the location where most of the echoic changes were observed. Several studies involving surgery have found that in the majority of cases the pathological process is localized in the proximal part of the tendon (4, 10, 17, 23, 24). Magnetic resonance imaging (MRI) studies have shown that the anteroposterior diameter of the normal tendons increases slightly from proximal to distal (27). Since stress/strain resistance is correlated with the cross-sectional area, this may explain why the pathological process usually starts in the proximal part of the tendon.

No difference in the tendon length or the modified Insall–Salvati index could be detected between symptomatic and asymptomatic groups of knees. This suggests that players with longer tendons are not predisposed to jumper's knee, in contrast to Kujela et al. (28, 29), who reported a significantly higher proportion with patella alta among those with jumper's knee compared to controls. However, their reports included far fewer volleyball players in the control groups than in the patient groups, and this fact may have skewed their results and reduced the external validity of their studies.

Conclusions

The relationship between symptoms and clinical findings of jumper's knee and the ultrasound changes was weak. Specific ultrasound findings could neither be used to predict the clinical grade of the disease, nor the duration of symptoms. Therefore, ultrasonography cannot be regarded as a diagnostic gold standard in the evaluation of patients with jumper's knee. More detailed information is needed on the pathophysiology of jumper's knee, in

particular in the early stages of symptom development.

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Paper III

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Characteristics of the Leg Extensors in Male Volleyball Players with Jumper's Knee

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ABSTRACT

The aim of the present study was to characterize the performance ability of the leg extensor apparatus in a group of athletes with jumper's knee and to compare the results with those of a matched control group without knee symptoms. Patient and control groups (12 players in each) were selected from a population of 141 well-trained male Norwegian volleyball players, of which 55 (39%) satisfied the diagnostic criteria for jumper's knee. The testing program consisted of a standing jump, a countermovement jump, a 15-second rebound jump test, a standing jump with a 20-kg load, and a standing jump with a load corresponding to one-half of the subject's body weight. Jump height and power were measured using a contact mat connected to an electronic timer. The test results of the patient group were significantly higher than those of the control group for the countermovement jump (15% increase), power during rebound jump (41%), work done in standing jump (12%) and countermovement jump (22%), and the difference between countermovement jump and standing jump (effect of adding eccentric component). Athletes with jumper's knee demonstrated better performance in jump tests than uninjured athletes, particularly in ballistic jumps involving eccentric force generation.

In a number of sports, athletes are required to perform jumping actions or rapid accelerations, thereby placing great demands on the knee extensor apparatus. Many of these athletes complain of pain at the distal or proximal insertion of the patellar tendon, or at the insertion of the quadriceps tendon. This syndrome of pain during and after activity was named "jumper's knee" by Blazina et al.[2] in 1973, but it is also referred to as patellar tendinitis.[3,4]

Athletes with jumper's knee are usually unable to recall one specific traumatic event that initiated the pain. It is therefore assumed that in most cases the injury results from repetitive overloading of the tendon fibers. Histologic findings of degeneration and fibrotic scarring in the tendon itself,[12,17,26,28–30] as well as in the bone-tendon junction[8] suggest that the injury consists of an unhealed partial tendon tear. This view is supported by the demonstration of abnormalities in the tendinous tissue using ultrasonography, computed tomography, and magnetic resonance imaging.[3,7,11,12,14,15,17,19,25,26]

Our understanding of the causes of partial ruptures of the patellar tendon is incomplete. Epidemiologic studies show that the prevalence of jumper's knee among volleyball players is related to the frequency of training sessions, and that the prevalence is higher among players training on hard surfaces.[10,27] Similar epidemiologic data from other sports is not available, and it is not known why some athletes have problems whereas others do well, despite an equally high training volume.

It is conceivable that an athlete who is able to generate a high impulse during takeoff when jumping or running is at risk of injury from high repetitive loads on the leg extensor apparatus. Thus, the aim of the present study was to characterize the performance ability of the leg extensors in a group of athletes with jumper's knee using a standardized program of jump and power tests and to compare the results with those of a matched control group.

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MATERIALS AND METHODS

Subjects

The Norwegian Volleyball Federation leagues consist of amateur teams from all of Norway, and the teams are separated into six divisions according to their levels of play. Division I and II consist of 16 men's teams with a total of 164 licensed players. Of these licensed players, 141 participated in two tournaments in September 1989, just before the start of the indoor season. These players were interviewed during the tournaments. The information requested from each player included age, height, weight, number of training hours per week during the preceding 6 months, weight training and jump training (plyometric training) done each week, warm-up and stretching habits, type of floor in their normal training gym, type of shoe normally worn during volleyball training, and data on present and former knee injuries.

All players with current knee complaints or a history of previous injury consented to go through a clinical interview and a standard knee examination. The following diagnostic criteria were used to identify jumper's knee: 1) history of pain in the quadriceps or patellar tendons or their patellar or tibial insertions in connection with volleyball play and 2) tenderness to palpation corresponding to the painful area. Previous incidences of jumper's knee were diagnosed based on history alone. Players with current symptoms of jumper's knee were encouraged to report at the testing station for jump testing if they satisfied the following criteria: 1) symptoms from the patellar tendon only, and 2) no history of intraarticular abnormalities (positive patella grinding test, positive meniscal tests, instability, locking, giving way, or joint effusion), rheumatic disease, previous fractures in the knee region, previous knee surgery, or previous corticosteroid injections in or around the patellar tendon.

The characteristics of the subjects with and without jumper's knee are shown in Table 1.

TABLE 1
Characteristics of Players With and Without Jumper's Knee (Values are Means ± SD)

Variable	Jumper's knee	
	With (N = 55)	Without (N = 86)
Age (yrs)	24.8 ± 4.2	24.6 ± 4.6
Height (cm)	189.0 ± 5.9	188.0 ± 6.5
Weight (kg)	82.2 ± 7.0	80.0 ± 8.2
No. of seasons played	8.5 ± 3.4	8.3 ± 4.0
No. of volleyball training sessions per week	4.4 ± 1.0[a]	3.9 ± 1.0
Weight training (hr/wk)	1.5 ± 1.4	1.2 ± 1.2
Jump training (hr/wk)	0.6 ± 0.8	0.4 ± 0.6
Warm-up time (min)	23 ± 10	22 ± 8
Stretching time (min)	7 ± 5	7 ± 5

[a] Significant difference between players with and without jumper's knee.

Testing Program

Twelve of the players who reported for jump testing satisfied the criteria for inclusion in the patient group and successfully completed the standardized jump testing program. A matched control group, consisting of 12 players with normal knee examinations and no history of knee pain, consented to undergo an identical testing program. The players in the control group were actively recruited among team members of the injured players. The players were individually matched with respect to age, position (middle blocker, outside hitter, setter), playing experience, and training level.

The testing program was performed using Ergojump equipment (KB Ergotest, Mikkeli, Finland), which consists of a contact mat connected to a computerized electronic timer.[4,5,20,31] The equipment measures the flight time of each jump, and the jumping height (in centimeters) is calculated from this. In addition, power was calculated from flight and contact times during rebound jumping.[5]

The jumps performed were the standing jump, the countermovement jump, the standing jump with a 20-kg load, the standing jump with a load corresponding to one half the subject's body weight, and the 15-second rebound jump test. As described by Komi and Bosco,[20] standing jumps are performed with the subjects starting from a stationary semisquatting position with the knees flexed 90°. No countermovement is allowed with any body segment, and the hands are kept fixed on the hips. In the countermovement jumps, the subjects start the movement from a stationary erect position with the knees fully extended. They then bend down to approximately 90° of knee flexion before starting the upward motion of the jump (Fig. 1). The 15-second rebound jump test consists of continuous countermovement jumps. The subjects are encouraged to jump as high and as fast as possible for 15 seconds. Rebound jumping is also performed with the hands fixed on the hips, and in each jump the subject squats down to approximately 90° of knee flexion.

The subjects were vocally encouraged during the tests and were watched carefully to ensure that the proper technique was used. In particular, care was taken to ensure that there was no countermovement in the standing jumps and that the subjects landed with straight legs. The best of three technically correct attempts was recorded and used for the statistical analysis, except for the 15-second rebound jump test, which was performed only once.

Data Analysis

Results are given as means ± SD unless otherwise noted. Patient and control groups were compared using unpaired t-tests. An alpha level of 0.05 was considered significant.

RESULTS

The characteristics of the patient and control groups are shown in Table 2. The players from the patient and control groups came from the same teams, used the same types of

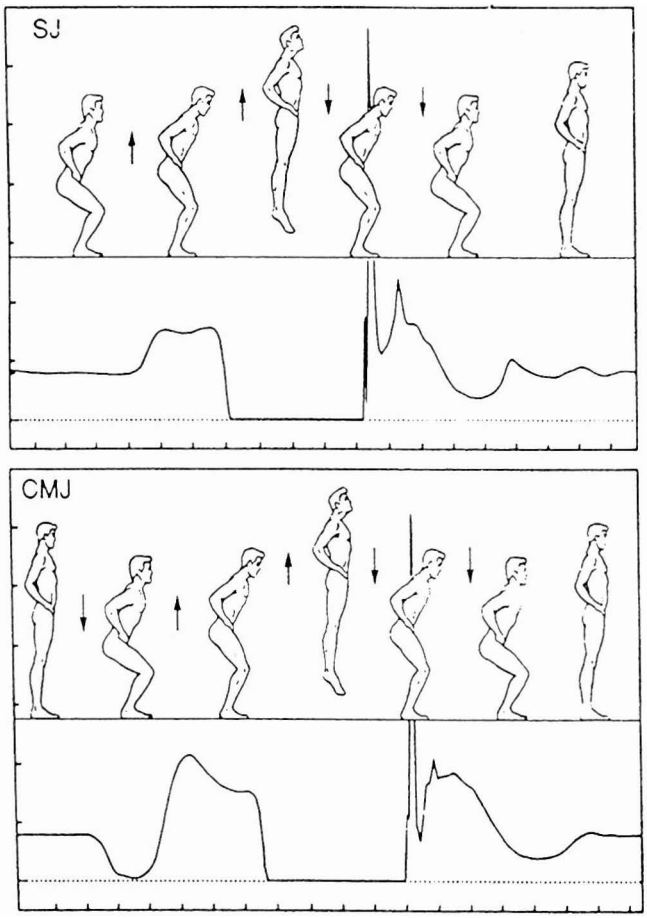

Figure 1. Data from typical force platform recordings (vertical ground-reaction force compared with time) during standing jumps (SJ) and countermovement jumps (CMJ). Jumps with loads (20 kg or one-half body weight) were done with the standing jump technique but with the subjects holding barbells on their shoulders. The rebound jumping test consists of continuous countermovement jumps for 15 seconds, with each jump performed as a maximal ballistic movement down to 90° of knee flexion.

shoes, and trained and played on the same type of gymnasium floor.

In the jump tests, the patient group performed better than the control group in the countermovement jump, the standing jump with a 20-kg load, and the 15-second rebound jump test (Table 3). Also, the work done in countermovement and standing jumps was greater in the patient group, as was the difference between jump height in countermovement and standing jumps (Fig. 2).

DISCUSSION

The main finding of this study was that a group of players with jumper's knee performed better in a standardized series of jump and power tests than a matched control group.

The high prevalence of jumper's knee among high-level volleyball players (30% to 40%) is assumed to be caused by the high number of jumps performed during training and games.[9,10,27] To our knowledge, no epidemiologic studies are available from other sports, but clinical studies suggest frequent problems in other team sports, such as soccer and basketball, and in athletics.[16,24,28,29] Volleyball involves approximately 60 maximal jumps per hour of play, and previous studies have shown that the prevalence of jumper's knee increases with increased frequency of training.[10,27] This finding is supported by the present study, which shows a small but significant difference in training volume between players with and without symptoms. The tactics of the game require middle blockers to jump more than other players, and it has been shown that they have a higher prevalence of jumper's knee.[27] Thus, there is ample evidence that the prevalence of jumper's knee in volleyball players is closely related to the amount of jumping.

However, it is not known why some players have problems whereas others do well despite an equally high training volume. Biomechanical evidence is limited, but there is no convincing evidence to support suggestions that injury may be associated with malalignment of the extensor mechanism of the knee, patella alta, abnormal patellar laxity, or other structural abnormalities.[21,22,34] Instead, we hypothesized that the problem may be related to the performance characteristics of the leg extensors. Players who jump well load their tendons more than others, and

TABLE 2
Characteristics of Patient Group and Control Group (Values are Means ± SD)

Variable	Patients (N = 12)	Controls (N = 12)
Age (yrs)	23.7 ± 3.0	24.8 ± 4.6
Height (cm)	189.3 ± 7.0	187.9 ± 4.9
Weight (kg)	84.1 ± 5.6[a]	79.2 ± 3.7
No. of seasons played	7.2 ± 2.2	8.5 ± 2.8
No. of training sessions per week	4.6 ± 1.2	4.3 ± 1.1
Weight training (hr/wk)	1.0 ± 1.0	1.0 ± 0.6
Jump training (hr/wk)	0.3 ± 0.7	0.5 ± 0.5
Warm-up time (min)	19 ± 7	20 ± 3
Stretching time (min)	6 ± 4	5 ± 3

[a] Significant difference between groups.

TABLE 3
Results from Jump Tests for Patient Group and Control Group (Values are Means ± SD)

Test[a]	Patients (N = 12)	Controls (N = 12)
SJ (cm)	40.1 ± 5.9	37.8 ± 3.4
CMJ (cm)	45.4 ± 5.5[b]	39.5 ± 3.4
CMJ − SJ (cm)	5.2 ± 2.7[b]	1.6 ± 1.4
SJ with 20-kg load (cm)	29.7 ± 3.1[b]	26.5 ± 1.8
SJ with 1/2 body weight load (cm)	22.4 ± 2.7	20.5 ± 2.4
Rebound jumps (W)	41.1 ± 9.8[b]	29.1 ± 10.3
SJ, work (J)	330 ± 48[b]	294 ± 33
CMJ, work (J)	373 ± 41[b]	306 ± 33

[a] SJ, standing jump; CMJ, countermovement jump.
[b] Significant differences between groups.

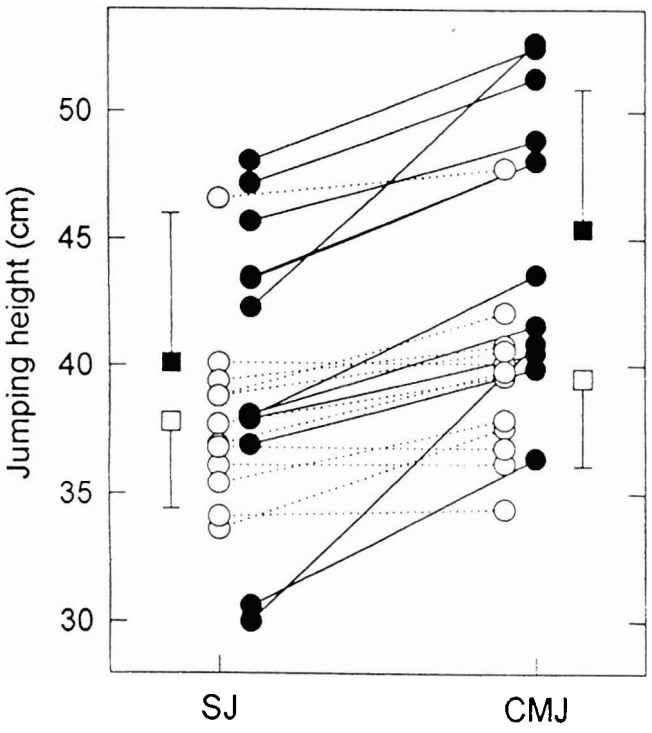

Figure 2. Individual (circles) and group (squares) values for the height of rise of the center of gravity (in centimeters) for standing jump (SJ) and countermovement jump (CMJ) in the group with jumper's knee (solid symbols) and the control group (open symbols). Group values are means ± SD.

this may lead to a greater risk of injury. Our data seem to indicate that this is the case.

The study design has some limitations that must be borne in mind when interpreting the results. It is possible that the selection of athletes to the patient group was biased, because ultrasonography was not available to confirm the diagnosis. However, we included only athletes with typical histories of patellar tendon pain in the patient group, and care was taken to exclude athletes with evidence of additional abnormalities. Also, matching control players from the same teams based on age, function, playing experience, and training level was thought to be the best way to minimize the risk of a selection bias. Although the study format allowed us to match the patient and control groups carefully with respect to diagnosis and factors believed to be of importance in the development of jumper's knee, it also resulted in a small sample size, and the results therefore need to be validated in a larger population of athletes.

The jump testing protocol is a standard program that has been shown to be highly reproducible.[31] The tests are functional and designed to give an estimate of performance at different speeds and loads, much in the same way that different demands are placed on the leg extensors for given tasks during the actual game of volleyball. The tests were familiar to the examiners as well as to many of the athletes; some teams used the same tests on a regular basis to check the efficacy of their training programs. Pain inhibition during jump testing among the players in the patient group is possible. The players did not express any problems and even if this occurred, it would appear not to invalidate the results. The patient group still performed better than the control group.

Numerous histologic studies[8,12,17,26,28–30] and studies using soft tissue imaging techniques[3,7,11,12,14,15,17,19,25,26] have shown abnormalities in the knees of patients with jumper's knee. These abnormalities may even progress to the point of a complete rupture[18] or near-complete ossification of the tendon.[13] The injury is usually situated at the bone-tendon junction, but more distal locations have also been described.[15,19] The histologic findings may be explained as consequences of a nonhealed, or insufficiently healed, partial rupture of the tendon.[15,29] It is assumed that the tendon responds with microruptures or gross tearing if the strength of the tendon is insufficient to meet the expectation of the applied forces.[33] The present study suggests that the risk of jumper's knee may be related to the load placed on the extensor apparatus during jumping, as evidenced by the differences in performance ability between those athletes with jumper's knee and those without. This finding is compatible with the concept of the injury being an unhealed partial rupture, as it is likely that the risk of tendon tears increases with load and not only with the frequency of training.

It is interesting that the test results did not differ between the groups for all modes of jumping. The standing jump is designed as a "pure" concentric movement, and the results for unloaded jumping did not differ between the groups. However, for the countermovement jump, which consists of a ballistic movement of a rapid eccentric muscle action immediately followed by a maximal concentric contraction, there was a significant difference between the groups (Table 3, Fig. 2). We also observed a significant difference in the 15-second rebound jump test, which consists of a series of ballistic jumping movements. Consequently, it may be assumed that the main difference between the groups was the way in which they were able to use the eccentric prestretch component of the ballistic motion to increase their jumping height. As can be seen from Figure 2, even the patients with relatively low standing jumps had a large increase when they were allowed to prestretch, whereas the control subjects who did relatively well on the standing jump were unable to increase their jumping height in a stretch-shortening type of movement. Eccentric force production is believed to be a primary cause of microruptures because eccentric force production may exceed conventional concentric and isometric forces threefold, and therefore also exceed the inherent strength of the tendon.[33]

Two mechanisms are suggested for the performance increase in coupled eccentric-concentric action compared with concentric action alone.[4] First, the ability to recruit more muscle fibers through reflex potentiation has been documented in EMG studies.[6] Second, it is believed that tendons, fasciae, and other elastic elements within muscle have the ability to store potential energy during the prestretch movement, which can then be released in the con-

centric phase.[6] It has recently been shown that musculotendinous stiffness differs between individuals, is related to performance ability, and can be influenced both by strength training and stretching.[35–37] Musculotendinous stiffness is likely to be related to tendon properties as well muscle properties, and it is therefore tempting to speculate that the tendons of injured athletes differ in elastic properties from controls. This hypothesis warrants further research.

For the injured athletes to have been able to jump higher than the control subjects, a larger vertical impulse must have been produced. Force was not measured directly in the present study, but it is likely that the force transferred through the patellar tendon was larger as well. From previous studies of volleyball players, it is known that good jumpers are characterized by a shorter contact time and higher peak force during takeoff.[32] Thus, the difference in peak force is likely to be larger than the difference in the jump result alone would seem to indicate. Also, there was a significant difference in body weight between the experimental groups (Table 2). Body composition was not determined, but regardless of whether the patients were more muscular or had larger fat deposits (not likely in this well-trained group of athletes), the weight difference would tend to further magnify the stress placed on the patellar tendon during jumping. Because more than 50% of the work done in jumping is produced by the knee extensors,[23] it seems reasonable to conclude that the differences observed in jumping height reflects a true increase in the force transfer through the patellar tendon.

The jumping ability of the players, 40 to 45 cm in a countermovement jump, may not seem impressive. However, the jumping mode tested differs from the techniques used when playing volleyball. In a spike jump players usually employ an approach run of two steps, a step-close takeoff technique, and a full arm swing, thereby adding another 55% to 65% to their countermovement result.[1] There is a close correlation between the results of a countermovement jump and a spike jump ($r = 0.96$),[1] and based on this relationship the spike jump of this group of injured players may be estimated to range from 55 to 92 cm.

The forces involved during takeoff and landing in actual play are also larger than during the standard test situation used in the present study,[1] but the biomechanical characteristics of the jumping techniques used in blocking and spiking in volleyball need to be examined in detail, particularly with reference to possible differences between uninjured and injured players. At this point we do not know whether problems are caused by takeoff or landing.

When comparing typical rehabilitation exercises with the forces and rates of force development incurred in eccentric-concentric contractions once the patient is returned to training and games, it is not surprising that treatment programs emphasizing immobilization, rest from athletic activity, or isometric exercises fail in patients with jumper's knee. Strength training must be specific to the proposed task of the tendon. As shown by Stanish et al.[33] and Karlsson et al.,[15] preliminary studies using specific eccentric training programs have shown promising results, even in patients with recalcitrant tendinitis. However, further studies are necessary to understand the forces involved in jumping so that proper rehabilitation training programs can be designed for injured high-performance athletes.

CONCLUSIONS

The performance characteristics of the leg extensors in a group of volleyball players with partial tears of the patellar tendon differed from those of a matched group of healthy athletes. Athletes with jumper's knee were able to jump higher, particularly in jumps involving eccentric force generation, presumably resulting in greater stress on the patellar tendon and an increased chance of partial tears.

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Paper IV

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Performance Characteristics of Volleyball Players with Patellar Tendinopathy

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Background: Patellar tendinopathy is assumed to result from chronic tendon overload. There may be a relationship between tendon pain and jumping ability.
Hypothesis: There is no difference in performance characteristics between volleyball players with patellar tendinopathy and those without.
Study Design: Prospective cohort study.
Method: We examined the performance of the leg extensor apparatus in high-level male volleyball players with patellar tendinopathy ($N = 24$) compared with a control group ($N = 23$) without knee symptoms. The testing program consisted of different jump tests with and without added load, and a composite jump score was calculated to reflect overall performance.
Results: The groups were similar in age, height, and playing experience, but the patellar tendinopathy group did more specific strength training and had greater body weight. They scored significantly higher than the control group on the composite jump score (50.3 versus 39.2), and significant differences were also observed for work done in the drop-jump and average force and power in the standing jumps with half- and full-body weight loads.
Conclusions: Greater body weight, more weight training, and better jumping performance may increase susceptibility to patellar tendinopathy in volleyball players.

Epidemiologic studies have shown a prevalence of patellar tendinopathy of 40% to 50% among high-level volleyball players.[6,8,19] No epidemiologic data are available on the prevalence in other sports, but results of clinical studies among patients undergoing surgical treatment for patellar tendinopathy suggest that there is a high prevalence among soccer players and in sprinters and jumpers as well.[13,20,23,24] Evidence from histologic and imaging studies suggests that the pathologic process involved consists of unhealed or incompletely healed microtears in the tendon substance, usually in the proximal part of the patellar tendon. The histologic changes are compatible with a degenerative condition without signs of inflammation.[5,7,9–12,14,21–25] Training volume and floor hardness are extrinsic factors that correlate with the prevalence of patellar tendinopathy.[8] Data on intrinsic factors are conflicting and mostly related to static biomechanical parameters.[8,16,17,19] In a previous case-control study, we evaluated some dynamic characteristics of the leg extensor apparatus, and the results suggest that players who have patellar tendinopathy perform better on jump tests than do healthy control subjects, especially on tests involving eccentric work.[18] The purpose of the present study was to examine the leg extensor characteristics in a larger cohort of players by using a more comprehensive jump- and strength-testing program.

MATERIALS AND METHODS

Study Design

This study was performed during an international volleyball tournament in Oslo, Norway, with approval from the ethics committee of the Norwegian Research Council. The tournament was played 2 months after the end of the ordinary competitive season, with teams competing in classes according to their level of play. The six Norwegian teams that participated in the men's elite class were invited

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to take part in the study. These were amateur teams that otherwise compete in the top division of the Norwegian Volleyball Federation (NVBF) leagues. The teams consisted of 53 players, and 47 of these (89%) consented to take part in an interview, clinical examination, and a series of standardized jump and power tests. Their patellar tendons were also examined ultrasonographically, and the results of this investigation have been presented in a separate article.[19]

Interview and Clinical Examination

Information requested from each player included age, height, weight, number of years participating in organized volleyball training, years of participation at the senior level and in the top division of the NVBF league system, number of training hours per week (volleyball training, weight training, and jump training), and stretching habits during the previous season.

Each player underwent a standard knee examination and clinical interview on present and former knee injuries and complaints. The following diagnostic criteria for patellar tendinopathy were used: history of pain localized to the lower patellar pole or insertion of the quadriceps tendon in connection with volleyball play and distinct palpation tenderness corresponding to the painful area.[1] A diagnosis of previous patellar tendinopathy was based on history alone. The subjects were classified according to criteria modified by Lian et al.,[19] based on Roels et al.[25] and Blazina et al.[1] (Table 1), and divided into two groups: those with current patellar tendinopathy and those with no history of patellar tendinopathy.

Jump and Power Testing

The players went through a standardized jump- and power-testing program. The testing program was performed by using a contact mat connected to a computer (Intervall A/S, Oslo, Norway) (Fig. 1). The equipment measures the flight time of each jump, and from this the height of rise of the center of gravity is calculated.[3,26] In addition, power can be calculated from flight and contact times during rebound jumps.[4]

The jumps performed were standing jump (SJ), counter-movement jump (CMJ), drop-jump from a dropping height of 45 cm ($DJ_{45\ cm}$), standing jump with a 20-kg load ($SJ_{20\ kg}$), standing jump with loads corresponding to one-half body weight ($SJ_{1/2\ bw}$) and full body weight ($SJ_{1/1\ bw}$), and a 15-second maximal rebound jump test (RJ). Standing jumps were performed with the subject starting from a stationary semisquatting position with 90° of knee flexion and with both hands kept fixed on the hips. No counter movement was allowed with any body segment. In the counter-movement jump the subject started the movement from a stationary erect position with knees fully extended, and was allowed to bend down to approximately 90° of knee flexion before starting the upward motion of the jump. Standing jumps with loads were performed with barbells on the shoulders of the players. The drop-jump was performed as a counter-movement jump, except that the player dropped from a height of 45 cm. In the 15-second maximal rebound jump test, the subjects were encouraged to jump as high and as fast as possible during 15 seconds (Fig. 1).[15]

The players were encouraged vocally during the jumps and were watched carefully to ensure that the proper

TABLE 1
Classification of Patellar Tendinopathy According to Symptoms[a]

Grade	Symptoms
I	Pain at the infrapatellar or suprapatellar region after practice or after an event
II	Pain at the beginning of the activity, disappearing after warm-up and reappearing after completion of activity
IIIa	Pain during and after activity, but the patient is able to participate in sports at the same level
IIIb	Pain during and after activity, and the patient is unable to participate in sports at the same level
IV	Complete rupture of the tendon

[a] Symptoms as outlined by Roels et al.,[25] Blazina et al.,[1] and Lian et al.[19]

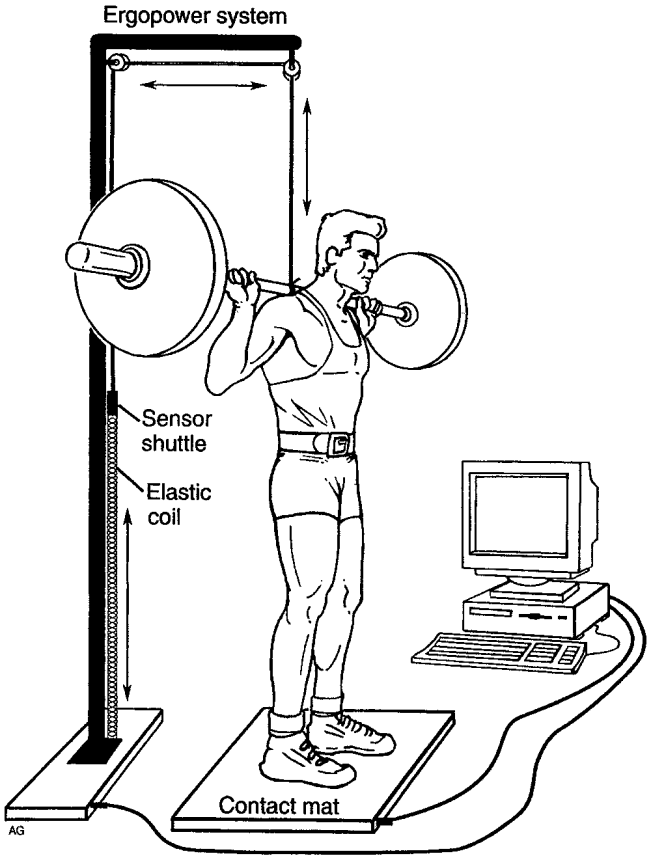

Figure 1. Schematic of the experimental setup for the jump tests. During all tests the players jumped on a contact mat connected to a computer, making it possible to compute jumping height.[4] Also, during jumps with an added load, the barbell was mechanically linked with the Ergojump system connected to a shuttle, making it possible to calculate force, velocity, and power.[2]

technique was used. In particular, care was taken to ensure that there was no counter movement in the standing jumps and that the subjects landed with straight legs. The best of three technically correctly performed jumps was used for the final calculations.

In addition, during the execution of the standing jumps with loads, the average velocity, force, and power during the jump were measured with the Ergopower system (Ergotest Technology AS, Langesund, Norway) (Fig. 1). The equipment measured the displacement of gravitational loads (in this case, barbells) as external resistance.[2] The vertical displacements of the loads were monitored with mechanical and sensor arrangements. The loads were mechanically linked to a shuttle gliding on a track bar. The movement of this shuttle was recorded by the sensor, which was interfaced to an electronic device that included a microprocessor and software. The microprocessor worked internally with a 10-μm time resolution. When the subject moved the loads, the signal from the sensor interrupted the microprocessor every 3 mm of displacement. Thus, it was possible to calculate velocity, acceleration, force, power, and work corresponding to the load displacements. This system has been shown to be accurate and reproducible.[2]

Data Analysis

For each player, a composite jump score to evaluate the performance ability of the leg extensor apparatus was calculated by rating each player's result on a scale from 0 to 100 on each of the jump tests, where 0 represents the lowest test score among all the players tested and 100, the best score. The overall score was computed as the average of the results from each of these eight scores. Results are given as means ± SD unless otherwise noted.

Prevalence was compared between the two groups by using chi-square tests. Comparisons of the jump and strength test results between the patellar tendinopathy group and the control group were made with unpaired *t*-tests. An alpha level of 0.05 was used.

RESULTS

Prevalence of Jumper's Knee

Of the 47 players participating in the study, 24 (51.0%) were given a diagnosis of current patellar tendinopathy affecting at least one side, based on the clinical examination (typical history and clinical findings). Twenty players (42.6%) had never experienced problems in either knee, whereas three players (6.4%) reported having had previous knee problems identified as patellar tendinopathy. The severity of symptoms among those with current patellar tendinopathy (33 knees) was classified as grade I in 6 knees, grade II in 18 knees, and grade IIIa in 9 knees (Table 1). The onset of symptoms was gradual in 31 knees (94%) and acute in 2 knees, and the duration of symptoms reported by the players who had patellar tendinopathy was 3.5 ± 2.4 years (range, 0.1 to 10). The age at symptom onset was 18.8 ± 2.8 years (range, 13.5 to 25.9).

Player Characteristics

The characteristics of the players and their training backgrounds are shown in Table 2. Players with a diagnosis of patellar tendinopathy had a significantly greater body weight than the control subjects and trained more with weights. The prevalence of current patellar tendinopathy was significantly higher among outside hitters (12 of 18, 67%) and middle blockers (9 of 14, 64%), compared with utility players (1 of 6, 17%) or setters (2 of 9, 22%).

Thirty-seven players (79%) reported using a right-left step-close takeoff technique in the spike jump, whereas 10 players (21%) used a left-right takeoff. Only 1 player reported preferring the right leg when landing after the attack, whereas 31 players (66%) reported a balanced landing technique, and 15 players (32%) reported favoring their left leg when landing. The takeoff and landing techniques among the players with current symptoms of jumper's knee are shown in Table 3.

TABLE 2
Characteristics of Players with Current Symptoms of Patellar Tendinopathy and Players with No History of Patellar Tendinopathy (Means ± SD)

Variable	Current symptoms (N = 24)	No history (N = 20)	Significance level (P)
Age (years)	22.4 ± 2.5	22.0 ± 4.0	0.65
Height (cm)	191.1 ± 7.0	189.5 ± 6.2	0.43
Weight (kg)	86.7 ± 7.9[a]	81.9 ± 8.1	0.05
Organized volleyball training (years)	8.0 ± 2.8	7.5 ± 3.6	0.55
Training at senior level (years)	6.8 ± 2.5	5.7 ± 3.6	0.28
Training at elite level (years)	2.5 ± 2.6	2.2 ± 3.2	0.70
Volleyball training (hours/week)	7.7 ± 2.1	7.4 ± 1.6	0.53
Weight training (hours/week)	4.5 ± 2.8[a]	2.3 ± 2.3	0.009
Jump training (hours/week)	0.4 ± 0.9	0.6 ± 1.1	0.53
Total training (hours/week)	12.6 ± 4.2	10.3 ± 3.9	0.06
Stretching during warm-up (minutes)	3.4 ± 3.0	3.1 ± 2.7	0.71
Stretching after training (minutes)	6.2 ± 5.8	7.1 ± 3.9	0.55

[a] Significantly different from players with no history of patellar tendinopathy (unpaired *t*-tests).

TABLE 3
Takeoff and Landing Technique in Spike Jump for each of the Knees with Patellar Tendinopathy (N = 33)

Technique	Right knee (N = 22)	Left knee (N = 11)
Right-left takeoff	20	11
Left-right takeoff	2	0
Right-left landing	0	0
Left-right landing	6	4
Simultaneous landing	16	7

Jump and Power Testing

The test results for players with current symptoms of patellar tendinopathy and players without a history of patellar tendinopathy are shown in Table 4. The patellar tendinopathy group scored significantly higher than the control group on the composite jump score (50.3 versus 39.2, P = 0.02), and significant differences were also observed for work done in the drop-jump and average force and power in the standing jumps with half- and full-body weight loads.

DISCUSSION

The main findings of the present study were that players with a clinical diagnosis of patellar tendinopathy generally performed better on the dynamic testing program than did players without patellar tendinopathy. The symptomatic group had a greater body weight and did more specific weight training than did those in the control group.

TABLE 4
Results of Jump and Power Tests in Players with Current Symptoms of Patellar Tendinopathy and Players with No History of Patellar Tendinopathy (Means ± SD)

Measurement and jump[a]	Current symptoms (N = 24)	No history (N = 20)	Significance level (P)
Jump height (cm)			
SJ	36.2 ± 5.8	36.0 ± 4.0	0.88
CMJ	41.3 ± 6.5	40.3 ± 4.1	0.54
CMJ–SJ	5.1 ± 2.1	4.3 ± 1.8	0.19
DJ_{45cm}	53.1 ± 7.1	50.5 ± 6.0	0.20
SJ_{20kg}	27.3 ± 5.1	26.6 ± 3.7	0.60
$SJ_{1/2bw}$	19.5 ± 4.4	18.3 ± 3.4	0.33
$SJ_{1/1bw}$	10.0 ± 2.3	9.5 ± 2.4	0.55
Work (J)			
SJ	306 ± 46	286 ± 34	0.14
CMJ	349 ± 56	322 ± 35	0.06
DJ_{45cm}	449 ± 67[b]	404 ± 53	0.02
Average power (W)			
Rebound jumps 15 s	67.4 ± 13.4	60.3 ± 11.5	0.07
$SJ_{1/2bw}$	705 ± 133[b]	621 ± 104	0.04
$SJ_{1/1bw}$	1048 ± 161[b]	865 ± 147	0.003
Average force (N)			
$SJ_{1/2bw}$	528 ± 47[b]	485 ± 49	0.01
$SJ_{1/1bw}$	1011 ± 83[b]	908 ± 70	0.001
Average velocity (m/s)			
$SJ_{1/2bw}$	1.33 ± 0.17	1.27 ± 0.14	0.28
$SJ_{1/1bw}$	1.03 ± 0.12	0.95 ± 0.14	0.10

[a] SJ, standing jump; CMJ, counter-movement jump; DJ_{45cm}, drop-jump from 45 cm height; SJ_{20kg}, standing jump with 20 kg weight; $SJ_{1/2bw}$, standing jump with loads corresponding to one-half body weight; $SJ_{1/1bw}$, standing jump with loads corresponding to full body weight.
[b] Significantly different from players with no history of patellar tendinopathy (unpaired t-tests).

Patellar tendinopathy is a condition characterized by histologic[7,10,12,22–25] and soft tissue imaging findings[5,9–12,14,21,22] compatible with an unhealed or insufficiently healed partial patellar tendon tear. These partial tears probably occur when the strength of the tendon is insufficient in relation to the applied forces.[29] The tendon may be subject to fatigue under the high chronic repetitive loading, despite the fact that the cyclical loads may be well within the ultimate failure stress range of the tendon,[28] which is in the range of 56.7 ± 4.4 MPa. This view is supported by the fact that most of the players with patellar tendinopathy reported a gradual onset of their symptoms. Because eccentric force production in certain circumstances may be three times the concentric force, it is believed to be a primary cause of the microruptures.[29] It has been suggested that tendon overload may result from a combination of extrinsic (such as floor type)[6,8] and intrinsic (such as malalignment) factors,[16,17] with the sum of these factors determining whether a player develops patellar tendinopathy.

In this study, we evaluated intrinsic factors with the jump-testing program. The composite jump score was designed as an overall indicator of a player's ability to load the extensor apparatus during conditions ranging from slow-speed concentric (standing jump with added load) to high-speed ballistic (rebound jumps) movements. The dynamic testing program was selected to resemble the various loading conditions imposed on the leg extensors during different jumping and cutting movements used in the game of volleyball. The significant difference in the composite jump score observed between the groups may be taken as an indication that the leg extensor apparatus in the group of players with patellar tendinopathy may be subjected to higher loads during volleyball play as well. There were significant differences between the players with current patellar tendinopathy and those without, both in average force and average power in standing jumps with added loads corresponding to one-half and whole body weight. Consequently, the forces acting on the tendon or the rate of force development during jumping may surpass the adaptive abilities of the tendon, and, in that way, cause microtears in the tendon substance among players with high performance ability.

In a previous case-control study, we found significant differences between two smaller groups of players in the results of a counter-movement jump, in the difference in jumping height between a counter-movement jump and a standing jump, and in a rebound test.[18] In this previous study the jumps were performed in the same manner as described in detail in the methods for the present study. However, we could not reproduce these results. The previous study included a smaller number of players, and in a case-control study it is possible that a selection bias may have occurred. However, the performance of the players with patellar tendinopathy in the first study in the counter-movement jump test and the rebound jump test

was significantly better than the results of the players in the present study. This suggests that the injured players in the first study had a highly developed leg extensor apparatus, which may indicate a stronger disposition to patellar tendinopathy.

Data from previous studies concerning other potentially important intrinsic factors are conflicting; these studies have mostly evaluated static biomechanical parameters. Ferretti[6] found no differences in sex, alignment of the knee, alignment of the extensor mechanism, position of the patella, characteristics of the tibial tuberosity, rotation of the femur, rotation of the tibia, degree of constitutional instability, characteristics of the foot, or morphotype between subjects with and without jumper's knee. On the other hand, Kujala et al.[16,17] found more leg-length inequality and patella alta in patients with patellar tendinopathy compared with controls, on the basis of standing radiographs. With use of the same group of subjects as in the present study, we found no difference in the length of the patellar tendon or the Insall-Salvati index when we compared patients with patellar tendinopathy and control subjects.[19]

Epidemiologic studies on extrinsic risk factors have shown that the hardness of the playing surface and an increased frequency of training sessions correlate positively with the prevalence of patellar tendinopathy.[6,8] As expected, we found no difference between the groups in the total amount of specific volleyball training because all of the players were selected from the same teams—a well-trained group with a similar training history. However, we do not have detailed information on the training history of the players at the time they were first injured. At that time there may have been differences in training volume or intensity that we were unable to detect in a cross-sectional study. Longitudinal studies are necessary to examine in detail how training programs may lead to tendon overload.

It can be argued that the additional weight room training and better jumping characteristics were a consequence of the symptoms because the athlete with tendinopathy could be expected to spend more time in the training room, strengthening and stretching the aching muscle-tendon group. We find it highly unlikely that a painful condition regarded as a chronic overuse injury should improve the jumping capacity of these athletes. None of the teams had a physical therapist or athletic trainer working systematically with them, and at the time there was no tradition of systematic weight training (eccentric strength training) to treat patellar tendinopathy. In fact, most of the players had received no treatment for their symptoms. We did find that the prevalence of patellar tendinopathy was significantly higher among outside hitters and middle blockers compared with utility players and setters. This is not surprising because outside hitters and middle blockers perform a much higher number of maximal jumps than do setters as a result of their function on the team.

The players with patellar tendinopathy reportedly trained more with weights than the others did. This additional weight training by itself indicates a higher total loading of the extensor apparatus, and the anticipated effect of this training would also increase muscle mass and jumping ability. This indication is supported by the fact that the players with patellar tendinopathy had a greater body weight than those without patellar tendinopathy. We did not examine body composition, but it is unlikely that the body weight difference observed was due to differences in body fat in such a well-trained population of players.

The right knee was affected twice as often as the left knee in the patients in the present study. The majority of the players used a right-left step-close takeoff technique, and only one player reportedly preferred the right leg when landing after the attack. In fact, 20 of the 22 players with current jumper's knee on the right side used a right-left takeoff technique. This finding suggests that a relationship may exist between the takeoff technique and patellar tendinopathy and that the forces sustained during takeoff may be of considerable importance. For a right-handed player to obtain proper alignment of the upper body for an effective spike, the preferred technique involves placing the right foot first in a position of about 45° of external rotation[27] (Fig. 2). When using this takeoff technique, the deceleration work is done mostly with the right leg, subjecting it to higher eccentric-concentric loading than the left leg. Also, when these high loads are imposed, the right leg may be in a state of functional malalignment. The preferred takeoff technique results in

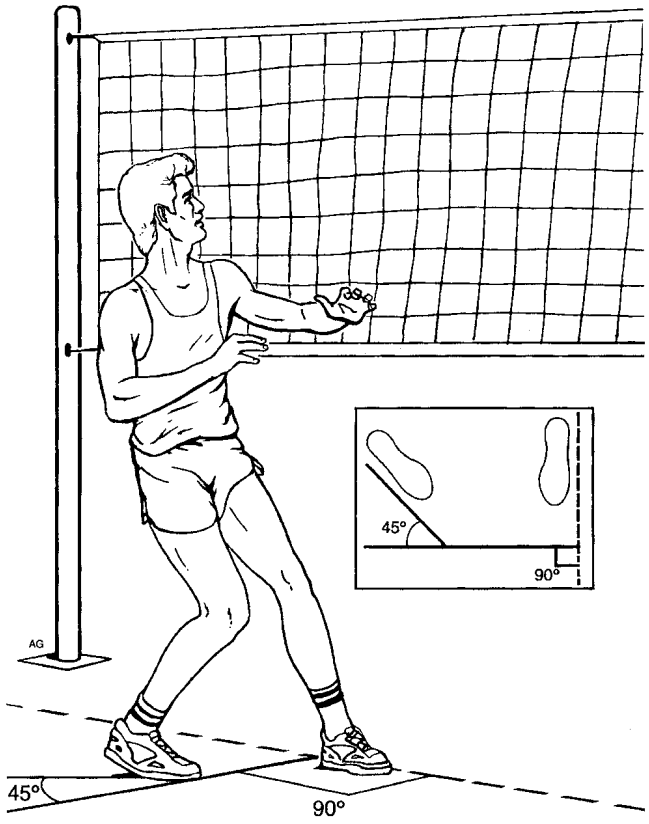

Figure 2. Takeoff technique during spike jumps in volleyball. Note how the typical foot placement pattern results in external rotation of the tibia in relation to the femur, increased knee flexion, and valgus stress on the right side.

a valgus position of the right leg, a greater flexion angle of the knee, and greater external rotation of the tibia relative to the femur (Fig. 2). It is possible that these factors result in a more unfavorable loading pattern of the right knee with respect to development of patellar tendinopathy. Motion analysis and direct force measurements are necessary to study this phenomenon in more detail.

It is tempting to speculate that the particular takeoff technique used in volleyball may cause loading patterns that are more likely to cause jumper's knee than those observed in many other sports. An exception may be high jumping, where the takeoff leg is loaded in valgus and external rotation, similar to the position in volleyball. However, the prevalence of jumper's knee in other sports is not known, although clinical studies indicate that jumper's knee may also be a problem among athletes in soccer and athletics.[13,20,23,24] The high prevalence of jumper's knee among high-level volleyball players detected in the present study is similar to that reported by others,[6,8,18] but further epidemiologic studies are necessary to compare the prevalence in other sports.

CONCLUSIONS

The overall results from the jump-testing program showed an increased performance ability of the leg extensors among players with a current diagnosis of jumper's knee compared with players without a history of jumper's knee. The body weight of the players with jumper's knee was also greater, and they reportedly did more weight training than the group without symptoms. All of these factors will tend to increase the loading of the extensor apparatus and thereby increase the susceptibility to partial tendon ruptures.

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Paper V

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Pronociceptive and Antinociceptive Neuromediators in Patellar Tendinopathy

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Background: The occurrence of nerve ingrowth and its relation to chronic tendon pain (tendinopathy) are still largely unknown. In healthy tendons, the innervation is confined to the paratenon, whereas the tendon proper is devoid of nerve fibers. In this study on the pathogenesis of tendinopathy, the authors examined sensory and sympathetic nerve fiber occurrence in the patellar tendon.

Hypothesis: Nerve ingrowth and altered expression of sensory and sympathetic neuromediators play a major role in the pathophysiology of pain in patellar tendinopathy.

Study Design: Case control study; Level of evidence, 3.

Methods: Biopsies from the patellar tendon in patients with patellar tendinopathy (n = 10) were compared with biopsies from a control group (n = 10) without any previous or current knee symptoms compatible with patellar tendinopathy. The biopsies were stained immunohistochemically for sensory and autonomic nerve markers. The biopsies from the 2 groups were compared using subjective and semiquantitative methods.

Results: Chronic painful patellar tendons exhibited increased occurrence of sprouting nonvascular sensory, substance P–positive nerve fibers and a decreased occurrence of vascular sympathetic nerve fibers, positive to tyroxin hydroxylase, a marker for noradrenaline.

Conclusion: The altered sensory-sympathetic innervation suggests a role in the pathophysiology of tendinopathy. Ingrowth of sprouting substance P fibers presumably reflects a nociceptive and maybe a proliferative role, possibly as reactions to repeated microtraumata, whereas the decreased occurrence of tyroxin hydroxylase may represent a reduced antinociceptive role. These findings could be used to develop targeted pharmacotherapy for the specific treatment of tendinopathy.

Keywords: tendon; pain; jumper's knee; substance P (SP); noradrenaline

Tendinopathy is a major cause of sick leave,[9] as well as morbidity related to athletic performance.[21] However, the basic pathogenesis of pain and degeneration in chronic tendon disease is generally poorly understood, which limits our ability to develop specific therapeutic interventions. In the absence of inflammation, the chemical and morphologic substrate for the experienced pain is also mostly unknown. However, neurogenic inflammation was recently implicated in the origin of achillodynia,[13] suggesting new therapeutic targets to mitigate symptoms.

Patellar tendinopathy is believed to be a tendon overload injury caused by a combination of internal and external risk factors.[29] Studies using Doppler flow technique[6,7,28] and histologic evaluations[25,26] have demonstrated increased blood vessel density in patients with degenerative tendon disease. Blood vessels cannot explain the pain suffered by these patients, and thus other factors related to pain pathophysiology, among them neuromediators, have been suggested[3,5,19,33] but are yet unidentified in patellar tendinopathy.

Recent observations have established that normal innervation of the tendon envelope (paratenon and surrounding loose connective tissue) consists of sensory and autonomic nerve fibers,[2,3,5] which are suggested to play an

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important role in the regulation of pain, inflammation, and tissue repair.[12,13,24,26] However, the healthy tendon proper is practically devoid of nerve fibers.[2,3,5] From other pain conditions, for example, low back pain, a relationship between sensory nerve ingrowth with expression of substance P (SP) in the disc and pathogenesis of pain has been shown.[16] Recently, SP was also demonstrated in Achilles tendinopathy.[5,10,33] In rheumatoid arthritis, a connection has been demonstrated between decreased sympathetic input (ie, low levels of noradrenaline) and decreased anti-inflammatory capability.[34]

However, in tendinopathy, the relative ratio of sensory and autonomic nerve fibers and their clinical relationship to pain have not been studied. Thus, in this study, we compared the occurrence of sensory and sympathetic nerve fibers between chronic painful patellar tendons and controls.

METHODS

Patient Groups

The patient group included athletes from different sports who were included in a prospective randomized trial comparing surgery with eccentric training.[8] The following diagnostic criteria were used for patellar tendinopathy: history of exercise-related pain in the proximal patellar tendon or the patellar insertion and distinct tenderness to palpation corresponding to the painful area.[11] To be included in the study, the patients had to have a clinical diagnosis of jumper's knee grade IIIB; that is, the patient had pain during and after activity and was unable to participate in sports at the same level as before pain.[22,32] In addition, the patient had to have thickening and signal changes on the MRI corresponding to the painful area to ensure that the biopsies were taken from the tendinopathic area. Patients had to have symptoms for a minimum of 3 months and be willing to undergo surgery. Subjects were excluded if they had a history of knee or patellar tendon surgery, inflammatory joint conditions, or degenerative conditions. Both knees were included if the patient had bilateral problems.

Each patient went through a standardized interview, and the information requested from each athlete included age, height, weight, and number of years participating in organized athletic training. Patients were asked to report the number of training hours per week during the competition season (sport-specific training, weight training, jump training, and other types of training). To assess the severity of the condition, the athletes with current patellar tendinopathy also self-recorded their symptoms and level of sports function using the Victorian Institute of Sport Assessment (VISA) questionnaire.[36] This brief questionnaire assesses symptoms, function, and the ability to play sport.[36] The maximal VISA score for an asymptomatic, fully performing individual is 100 points, and the theoretical minimum is 0.[36] The VISA questionnaire has shown excellent short-term test-retest reliability and has been shown to be a valid measure of symptoms in patients with patellar tendinopathy.[36]

The control group was selected from patients with tibia fractures from low-energy trauma treated with marrow nailing. These patients could have no current or previous knee symptoms compatible with patellar tendinopathy. Subjects in both groups had to be at least 18 years old (to ensure that the epiphyses were closed) and able to understand oral and written Norwegian.

Exclusion criteria in both groups were previous surgical treatment in or around the same knee, corticosteroid injections in or around the same knee, serious traumatic injury affecting the same knee, any rheumatic disease, and degenerative knee disorders. The study was approved by the regional committee for research ethics, participation was voluntary, and consent was obtained.

Surgical Technique

The surgical exposure was identical in the 2 groups, with a 5-cm longitudinal midline or lateral parapatellar incision, splitting of the paratenon, and exposure of the patellar ligament. The paratenon was split longitudinally, any pathologic paratenon tissue was removed, and the tendon was fully exposed. In both groups, the biopsies were taken from the proximal bone-ligament junction. The tendon tissue was excised using a full-thickness wedge-shaped incision, wide from the patellar pole and narrowing distally. In the patient group, all abnormal tissue was removed. If clearly abnormal tissue was not seen macroscopically, the excision was based on the MRI signal changes. Typically, a wedge with a proximal base 1 cm wide and extending to an apex 20 to 30 mm distal from the patellar pole was removed. In the control group, the biopsies were taken with a width of at least 5 mm and a length of at least 20 mm from the middle portion of the ligament starting at the bone-ligament junction.

Biopsy Procedure

The biopsy handling was identical in the 2 groups. Immediately after the surgical procedure, the biopsies were transferred to Zamboni solvent.[38] The biopsies were stored in this solution for 4 to 24 hours and then washed in 0.1-M phosphate-buffered saline (PBS), pH 7.2, with 15% sucrose (weight/volume) and 0.1% natriumazide. This washing was done until the yellow color from the Zamboni solution could no longer be seen in the PBS solvent. The biopsies were then stored in PBS at 4°C for a minimum of 48 hours.

The samples were sectioned at 154 μm on a Leitz cryostat, and frozen sections were mounted directly on SuperFrost/Plus glass slides, 3 sections per slide, and stained using the avidin-biotin or the hematoxylin and eosin systems, for immunohistochemistry and light microscopy, respectively.

Morphologic Study. The hematoxylin- and eosin-stained slides were subjectively assessed by a single blinded observer and graded according to the Bonar scale[15] with regard to tenocyte morphologic characteristics and vascularity (Table 1).

TABLE 1
Modified Bonar Scale[a]

	Grade			
	0	1	2	3
Tenocytes	Inconspicuous, elongated, spindle-shaped nuclei with no obvious cytoplasm at light microscopy	Increased roundness; nuclei becomes ovoid to round in shape without conspicuous cytoplasm	Increased roundness and size; the nucleus is round and slightly enlarged; a small amount of cytoplasm is visible	Nucleus is round and large, with abundant cytoplasm and lacuna formation (chondroid change)
Blood vessels	Inconspicuous blood vessels coursing in between bundles	Occasional cluster of capillaries; less than 1 per 10 high-power fields	1-2 clusters per 10 high-power fields	More than 2 clusters per 10 high-power fields

[a]See Cook et al.[15] The scale is a semiquantitative tendon score based on tenocyte and blood vessel morphologic characteristics (grading of ground substance and collagen is not included in this reproduction).

Immunohistochemistry. The slides were rinsed for 10 minutes in PBS. Incubation with 10% normal goat serum in PBS for 30 minutes blocked nonspecific binding. Subsequently, the sections were incubated overnight in a humid atmosphere at +8°C with primary antisera for protein gene product 9.5 (PGP, 1:10 000, UltraClone, Wellow, United Kingdom), SP (1:10 000, Peninsula Laboratories, San Carlos, Calif), and tyrosine hydroxylase (TH, 1:5000, Peninsula Laboratories), a rate-limiting enzyme reflecting the occurrence of noradrenaline. The PGP is the carboxyl-terminal hydrolase to the ubiquitin protein, which is an important protein component in the axonal neurolemma and is used as a general nerve marker, which makes it possible to identify the total number of nerve fibers.[17,24,37] After incubation with the primary antisera, the sections were rinsed in PBS (3-5 minutes) and then incubated with biotinylated goat antirabbit antibodies (1:250, Vector Laboratories, Burlingame, Calif) for 40 minutes at room temperature. Finally, the sections were incubated for 40 minutes with Cy3-conjugated avidin (1:5000, Amersham International, Stafford, United Kingdom). Control staining was performed by omitting the primary antiserum. A Nikon epifluorescence microscope (Eclipse E800, Nikon, Yokohama, Japan) was used for the analyses. The slides were examined by 2 independent observers, who were blinded with regard to the group to which the slides belonged. The occurrence and neuromorphology of PGP, SP, and TH were subjectively assessed, and pictures were taken for subsequent semiquantitative analyses.

Semiquantitative Analysis. After the subjective assessment, the following steps identified in an earlier study[1] were applied to optimize the semiquantitative analysis: The patellar tendons were longitudinally sectioned, and the sections were numbered consecutively from the dorsal to the ventral aspect. Three sections from different levels (ie, ventral, middle, and dorsal parts of the tendon) were chosen to represent the full thickness of the tendon. Staining was performed simultaneously for all sections to be compared. For microscopic analysis, a video camera system (DXM 1200, Nikon) was attached to the epifluorescence microscope and connected to a computer. From each section, 3 images from the microscopic fields (× 20 objective) exhibiting the strongest immunofluorescence were stored in the computer. Thereafter, the images were analyzed using Easy Analysis software (Technooptik, Skarholmen, Sweden). The software denotes and considers all positively stained nerve fibers beyond a defined threshold of fluorescent intensity. The results were expressed as the fractional area occupied by positive fibers in relation to the total area. The fluorescent/total area was determined in 9 images in each biopsy of the patient and control groups, respectively. In the microscopic analysis, the mean interobserver coefficient of variation was 9.8% and the intraobserver variation 9.6%. For statistical analysis, the mean fluorescent/total area was calculated for each of the 10 biopsies from both the patient and the control groups.

Data Analysis

For continuous variables, the results are given as means with range, unless otherwise noted. Comparisons between groups were done using unpaired t tests, as noted in the "Results" section. An α level of .05 was considered significant.

A sample size analysis based on the results of earlier immunohistochemical semiquantification studies, using an estimated average of 0.65 and 1 and an SD of 0.3 and 0.4 in the 2 groups, respectively, as well as an α level of .05 and a β level of .30, resulted in a sample size of 10.

RESULTS

The mean age was 30 years (range, 24-34 years; n = 10) in the patient group and 29 years (range, 19-43 years; n = 10) in the control group. In the patient group, the mean number of years participating in organized training was 17 (range, 10-28 years; n = 10), and the mean number of total training hours per week was 14 (range, 6-24 hours; n = 10). The mean VISA score was 42 (range, 15-65; n = 10), and the

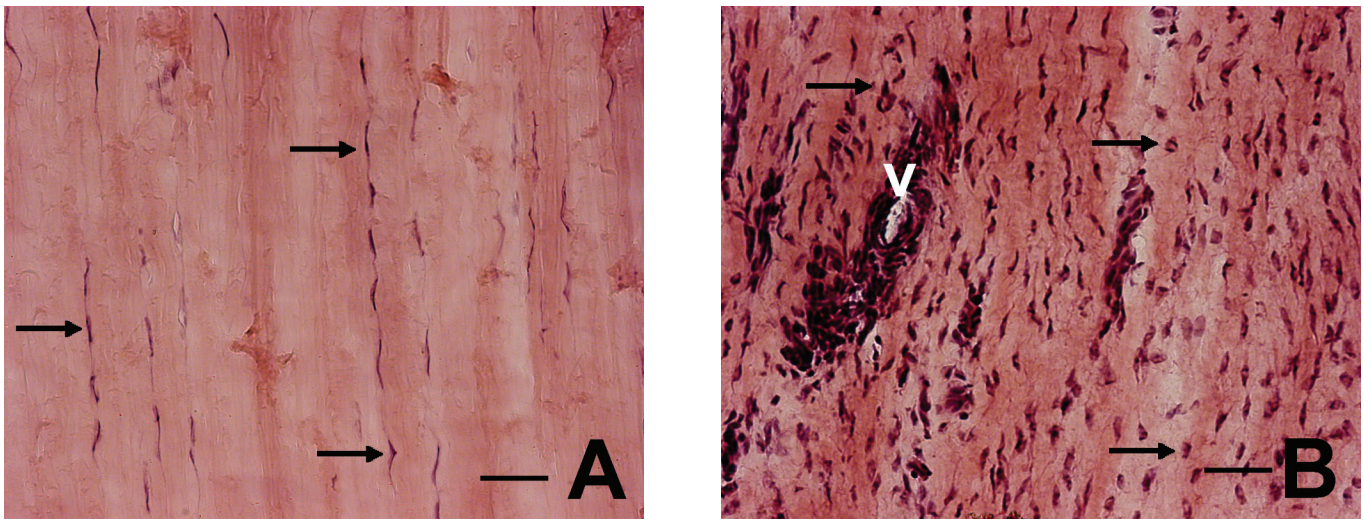

Figure 1. Hematoxylin and eosin micrographs of longitudinal sections through the patellar tendon of healthy control (A) and painful tendinopathy (B). Arrows denote tenocytes. The healthy tendon is homogeneous, with organized parallel collagen structure and thin, elongated tenocytes (A). The tendinopathy, on the other hand, is marked by collagen disorganization, increased cell count, activated tenocytes, and vascular ingrowth (V) in the tendon proper (B). Bar, 50 μm.

mean duration of symptoms was 36 months (range, 5-120 months; n = 10).

Microscopy

The morphologic appearance of the painful tendons in the tendon proper differed significantly compared with the appearance of the controls. The proper tendinous tissue exhibited signs of tendinosis (collagen degeneration, fiber disorientation, hypercellularity, angiogenesis, and absence of inflammatory cells) in all but 1 of the patients, whereas only a few of the controls exhibited early signs of tendinosis (Figure 1).

Semiquantitative assessment of tenocyte morphologic characteristics and of angiogenesis according to the Bonar scale, as signs of early and later stages of tendinosis, respectively, was performed.[15] Tenocyte changes occurred in all but 1 of the painful tendons, whereas only 3 of 10 controls exhibited these changes ($P = .006$). Angiogenesis, considered to be the last histologic sign of tendinopathy,[15] was found in 4 of 10 painful tendons but in none of the controls ($P = .038$).

Immunohistochemistry

Overall, the subjective immunohistochemical assessment confirmed the morphologic appearance. However, it also provided more detailed information about sensory (SP) and sympathetic (TH) nerve fiber occurrence in the patellar tendon. Thus, the majority (7/10) of the painful tendons exhibited an increased number of nerve fibers positive to SP and notably decreased levels of TH.

Sensory Nerves

Closer subjective analysis showed that the increased number of SP-positive fibers in the painful tendons occurred mainly as thin, varicose, sprouting nonvascular nerve terminals within the tendon proper (Figure 2B). Notably, these SP-positive nerves in the painful tendons were found over a larger area, more spread out within the tendon than in the controls. The SP-positive nerve fibers, seen as free nerve endings interspersed between the proper collagen fibers, often accompany the loose connective tissue ingrowth within the tendon proper of the painful tendons. Contrary to what one might have expected, no differences were noted between the groups regarding the small subpopulation of vascular SP-positive fibers. In both groups, SP was regularly seen in larger nerve bundles (Figure 2A).

Sympathetic Nerves

Subjective analysis demonstrated a great difference not only in the occurrence of TH-expressing nerve fibers between patients and controls but also in their morphologic distribution. In both groups, TH-positive nerves were present as free nerve endings throughout the tendon proper, but unlike the sensory nerves, the majority of the TH-positive nerves were distinctively related to the blood vessels (Figure 3A). In the patients, there was a distinct decrease in the occurrence of TH-positive nerves. Some TH-positive free nerve endings were still seen, but the vessel-related TH nerves in the patients were significantly diminished (Figure 3B).

General Nerve Occurrence

The neuronal localization of SP and TH staining was confirmed by positive immunoreactivity for PGP, a general nerve marker. The subjective analysis of PGP showed a distinctively higher nerve fiber occurrence in the chronic pain group compared with the controls. Nerves existed as

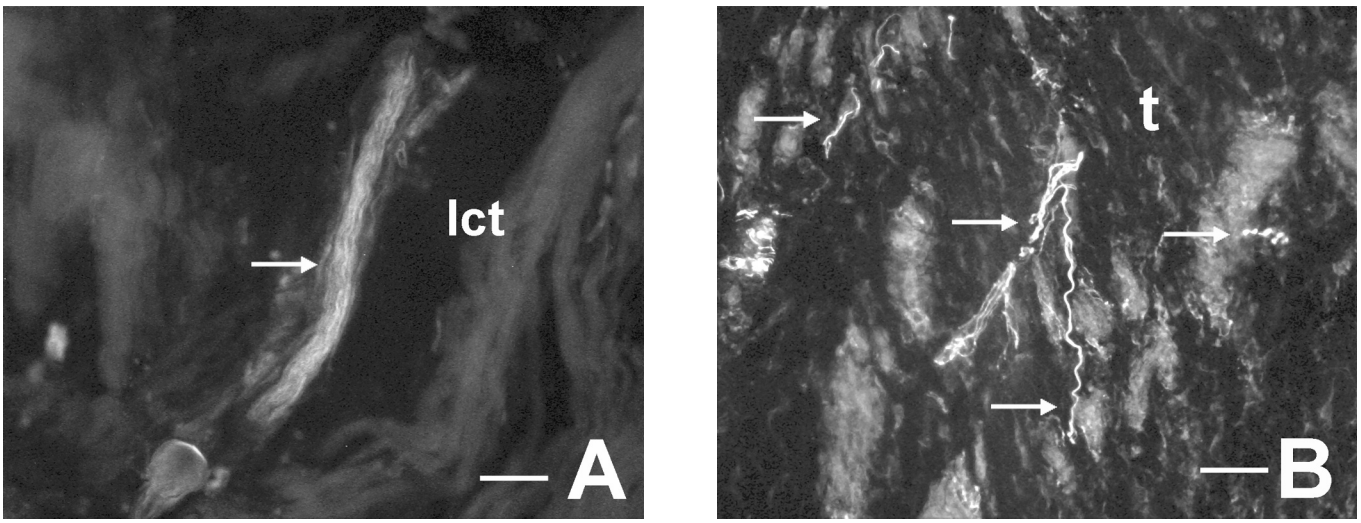

Figure 2. Immunofluorescence micrographs of longitudinal sections through the patellar tendon of healthy control (A) and painful tendinopathy (B) after incubation with antisera to substance P (SP). In the control tendon, SP-positive nerve fibers are mainly present as vascular nerve fibers and as large bundles (arrow) in the loose connective tissue (lct; A). In painful tendinopathy, increased spread and sprouting of SP-positive nerve fibers (arrows) are seen (B). These sprouting nerves even invade the tendon proper (t). Bar, 50 μm.

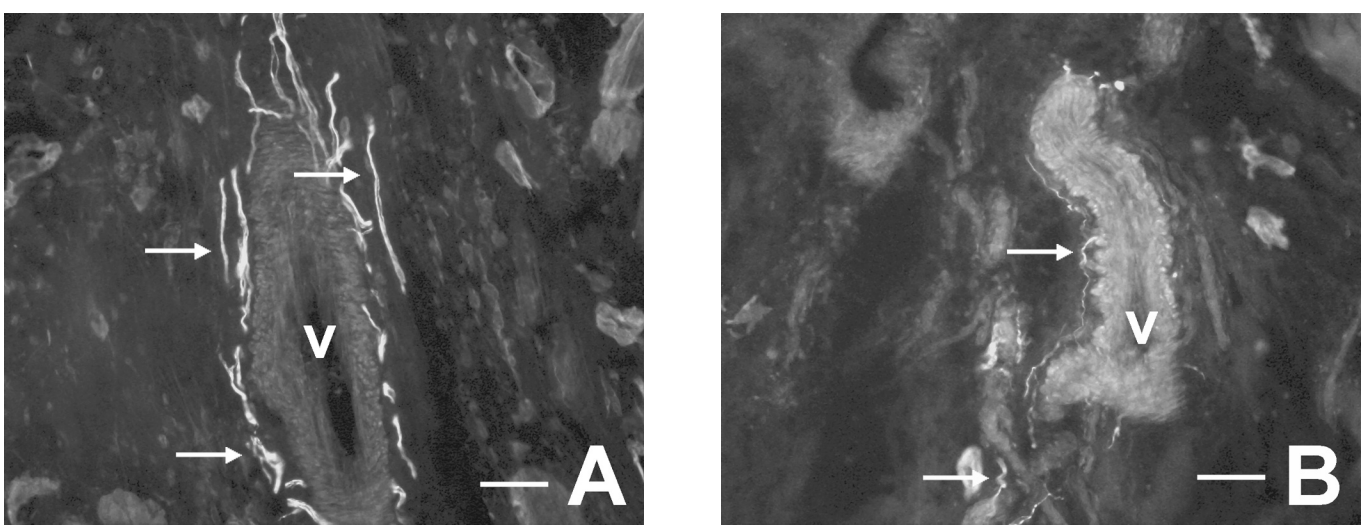

Figure 3. Immunofluorescence micrographs of longitudinal sections through the patellar tendon of healthy control (A) and painful tendinopathy (B) stained for tyrosine hydroxylase (TH, a marker for noradrenaline). Arrows denote nerve fibers. In the healthy tendon, a strong relation is seen between blood vessels and TH-positive nerves (A). In painful tendinopathy, a decreased number of TH-positive nerves, which are blood vessel related, are seen. V, blood vessel. Bar, 50 μm.

both vascular and nonvascular free nerve endings and in larger bundles.

Semiquantitative Immunohistochemistry

Computerized image analysis of SP, TH, and PGP expression showed similar differences in occurrence as assessed subjectively, although not all results were significant. The occurrence of SP was 22% ($P = .567$) and that of PGP 54% ($P = .098$) higher in the chronic painful tendons than in the controls. The occurrence of TH in the chronic painful tendons was 53% lower than in the controls ($P = .018$) (Figure 4).

DISCUSSION

This study demonstrates that the composition of nerve fibers expressing sensory (SP) and sympathetic neuromediators (TH) appears to differ between patients with painful

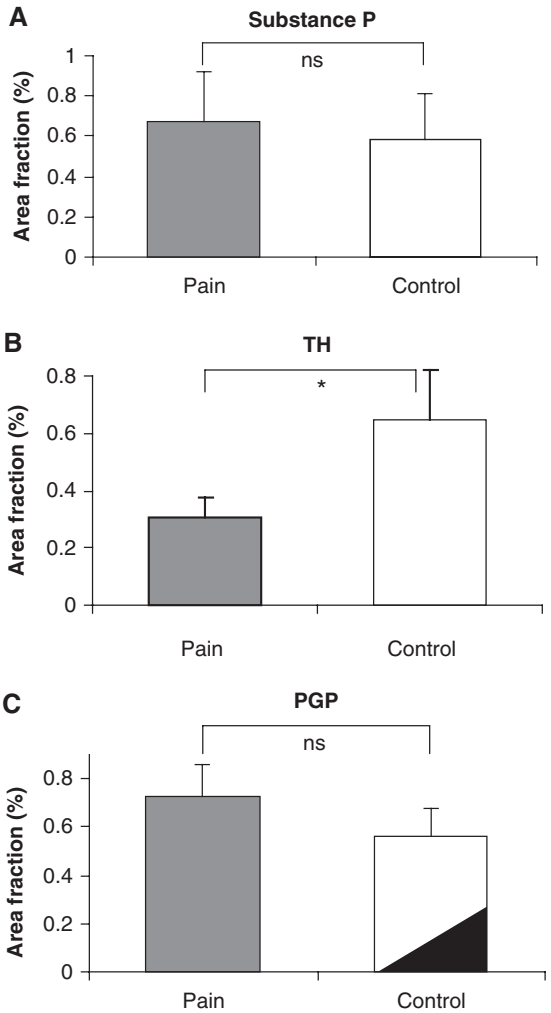

Figure 4. Mean area fraction occupied by nerve fibers (%) immunoreactive to SP (A), TH (B), and PGP (C) in painful patellar tendons as compared with controls (± standard error of the mean). *$P < .05$. Not significant (ns), $P > .05$. SP, substance P; TH, tyrosine hydroxylase; PGP, protein gene product.

patellar tendinopathy and controls. Most notably, a painful tendon is characterized by an increased number of SP-positive nonvascular nerve endings and a vascularly related decrease in TH, a marker of noradrenaline.

Tendinopathy is defined as a chronic and painful tendon disorder. The patients of this study had a mean symptom duration of 3 years and a VISA score of 42, which indicates a high level of pain and significant disability.[36] All patients exhibited transformed tenocytes, in contrast to only 3 of 10 controls. Angiogenesis, considered to be an advanced histologic sign of tendinopathy,[15] was found in 4 of 10 painful tendons but in none of the controls. This means that the histopathologic findings in this study can be interpreted as characteristic of a patient group with chronic and severe complaints of patellar tendinopathy. We do not know the activity level in the control group, but because the described histopathologic changes are assumed to be typical of a chronic overload injury, we do not expect to find these changes in asymptomatic tendons. However, from a methodological point of view, this possibility cannot be completely excluded.

The altered peripheral sensory-sympathetic innervation in patients suggests a role in the pathophysiology of tendinopathy.[31] Increased ingrowth of sensory nerves into the painful tendon proper, seen as sprouting free nerve endings, may explain the pain by reflecting intensified nociceptive transmission as a response to, for example, repetitive mechanical stimuli. The sympathetic nerves that are believed to act antinociceptively exhibited a reduced occurrence in the patients studied, thus supporting the notion that the observed changes in peripheral innervation are involved in the regulation of tendon pain.

The peripheral nervous system is known to react to outer and inner stress. It has been demonstrated that sensory nerve ingrowth and decreased sympathetic innervation occur as a response to tendon injury,[4] indicating that repeated microtrauma might be an initiator of the neuronal response. Moreover, the same study established that nociception during early healing is related to increased sensory and decreased autonomic neuromediator occurrence.

In this study, we focused on SP and not on calcitonin gene-related peptide because the research on SP is further advanced compared with that on calcitonin gene-related peptide. Thus, the relationship between SP and chronic pain is more established, also with regard to tendinopathy and tendon healing.[14,23,33]

The increased occurrence of SP in tendinopathy may reflect a multitude of actions. Substance P has been found to participate in inflammatory actions like vasodilation, plasma extravasation, and release of cytokines, in addition to its role in nociception, where SP has been reported to directly stimulate nociceptor endings in an autocrine/paracrine manner.[35] Similar actions may be presumed to occur in tendinopathy because it has been demonstrated that SP receptors are present.[23] The existence of SP within the tendon proper of the painful patellar tendons was in fact observed mainly in free nerve endings, indicating that the main function of SP in tendinopathy is nociceptive rather than vasoactive.

The reduction in TH, that is, vasoregulatory noradrenaline, suggests a suppressed antinociceptive function. A recent report has demonstrated that noradrenaline release leads to secretion of opioids from leukocytes.[30] Notably, a similar pattern of decreased vascular TH and increased free SP-positive nerve fibers is seen in patients with painful rheumatoid arthritis.[34]

In addition, the up-regulation of SP seen within the pathogenic tendon proper might reflect a trophic role. Substance P has in fact been shown to stimulate proliferation of fibroblasts[14] and endothelial cells,[27] as well as the production of transforming growth factor β in fibroblasts.[20] It is therefore tempting to speculate that SP contributes to the morphologic changes observed in tendinopathic patients, that is, tenocyte transformation, hypercellularity, and presumably neovascularization. Whether neuronal and cellular alterations in tendinopathy can be correlated requires further studies. It remains to be seen if the pain level is related to the ratio of SP to TH or to the degree of neovascularization.

The protracted presence of SP in tendinopathy is pathologic, in contrast to its trophic role in normal tendon healing. For progression of normal tendon healing, it has been shown that a strict temporal orchestration of neuromediator occurrence is essential. Thus, an initial up-regulation in SP at the healing site during the inflammatory and regenerative phases is followed by disappearance of SP and emergence of TH, representing a progress of healing.[4] However, in tendinopathic patients, the normal healing process appears to be at a standstill, characterized by high levels of SP and low levels of TH. Considering the similarities to rheumatoid arthritis,[34] increased SP expression in tendinopathy might even be part of a neuroinflammatory process. The classic vessel-related proinflammatory actions of SP may occur in the tendon envelope, that is, the paratenon and loose connective tissue, as demonstrated by an experimental study, whereas in the tendon proper, no classic inflammation was seen.[13] These observations are similar to the mostly free SP nerve endings seen in the current study. The prolonged release of SP from free nerves in the painful tendons may, as a neuroinflammatory process, suppress the synthesis of growth factors and increase the levels of stromelysin (endopeptidase, metalloproteinase) in the tendon.[18] Hence, the demonstrated up-regulation of SP might lead to subsequent matrix destruction in the pathogenic tendon proper.

In this study, the variation between biopsies was high, and the semiquantitative analysis confirmed only 1 of the 3 subjective analyses of the neuromediators in question. However, the trends all pointed in the same direction. The semiquantitative method takes only the fields with highest density of immunofluorescence into account, thus overlooking histologic differences, such as extensive nerve sprouting. The semiquantitative analysis should therefore only be regarded as a complement to the subjective analysis. Although the up-regulated SP occurrence was demonstrated exclusively by subjective analysis, the observations were corroborated by a recent report on Achilles tendinosis demonstrating increased SP levels in tendinopathy.[33]

In conclusion, this study demonstrates a differentiation in the sensory and sympathetic neuromediator pattern in patients with painful tendinopathy. The dominance of nonvascular SP nerve endings as well as the decrease of the antinociceptive modulator noradrenaline suggest a pathophysiologic up-regulation of pain. Both these neuropeptides, known to be essential for normal healing, exhibit a disturbed balance that may contribute to the degenerative and painful processes of tendinopathy. The understanding of the neuronal pathomechanisms may suggest new therapeutic targets to mitigate the symptoms in patients with painful tendon disorders.

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Paper VI

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Excessive Apoptosis in Patellar Tendinopathy in Athletes

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Background: The pathogenesis of tendon overuse injuries is poorly understood. The histopathology underlying tendinopathy at various anatomical locations is similar and may reflect a common pathologic process.

Hypothesis: Apoptosis contributes to the pathophysiology in patellar tendinopathy.

Study Design: Case control study; Level of evidence, 3.

Methods: We compared biopsy specimens from the patellar tendon in patients with patellar tendinopathy diagnosed clinically and with typical magnetic resonance image findings with biopsy specimens from a control group without any previous or current knee complaints to suggest patellar tendinopathy. The presence of apoptosis was examined with immunohistochemical methods using a polyclonal antibody recognizing active caspase-3, confirmed by labeling DNA strand breaks (F7-26 antibody) and nuclear morphology (fragmentation and condensation).

Results: The number of apoptotic cells per unit area (4.5 mm^2) was 0.91 ± 0.81 (SD) in tendinopathic samples and 0.21 ± 0.21 in controls (P = .026). Although the tendinopathic samples displayed increased cellularity (average 162.5 nuclei/mm^2 vs 98.9 nuclei/mm^2), the apoptotic index was higher (0.42% vs 0.17%, P = .014).

Conclusion: Increased apoptotic cell death is a feature of patellar tendinosis. The role of apoptosis within the broader framework and time course of tendon overuse injury remains to be established.

Keywords: tendon; patellar tendinosis; apoptosis

Overuse tendon injury—tendinopathy—is a common, recalcitrant problem in sports medicine. It has major effects on quality of life for competitive and recreational athletes.[4,25] Despite the currently available treatment options,[10,15,18,29,32] the condition can be career-ending.

Patellar tendinopathy is considered to result from tendon overload caused by internal and external factors. Regarding external factors, Ferretti et al[16] showed that there is a linear relationship between training volume and prevalence of tendinopathy among volleyball players, and that the harder the floor type on which they train, the higher the prevalence of patellar tendinopathy. In a recent epidemiological study among high-level athletes in sports with different quadriceps loading patterns,[25] the prevalence varied between sports—from no cases in cycling and orienteering to 32% and 44% with current symptoms in male basketball and volleyball, respectively.[25] It should also be noted that the mean duration of symptoms was more than 2 years, and that the affected athletes reported significant pain and reduced function levels.[25] Studies on internal pathogenic factors also indicate that athletes who subject the tendon to higher loads are at higher risk for tendinopathy.[26,28] However, the pathophysiological processes occurring within the tendon substance are mostly unknown, and there is a need for further studies.[1]

Tendons are characterized by a homeostatic balance, as in all other living tissues, with both inhibitory and stimulatory growth and survival signals.[8] It has been suggested that the earliest identifiable morphological changes in tendinosis occur in the tenocytes, not the collagen fibers.[11,44] One of the striking histological findings in biopsy specimens from tendinopathic tendons is the scarcity of inflammatory cells and a consistent histopathological picture featuring abnormal

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tenocyte shape and density, along with accumulation of glycosaminoglycans and collagen fiber thinning and disarray, with or without neurovascular proliferation.[11,19,21,22,30] Apoptosis, also called "programmed cell death," is a specific response to both physiological and stressful stimuli and is characterized by distinctive morphological and biochemical changes.[24,37] If the tenocyte is involved in the primary pathological changes, this may be compatible with a degenerative, apoptotic process.[44] Alternatively, apoptosis is commonly associated with late-stage remodeling of reparative tissue.[17,34]

In ruptured human rotator cuff specimens, Yuan and colleagues[43] reported excessive apoptosis using Terminal Deoxynucleotidyl Transferase Biotin-dUTP Nick End Labeling (TUNEL) and DNA laddering assays. The authors concluded that in this end-stage tendon disease in older individuals (average age 61 years), apoptosis was clearly present. Nevertheless, their study design did not allow them to determine whether apoptosis was present before or only after rupture. In addition, the effects of aging, anatomy, and vascular supply limit the ability to extrapolate to other tendons. Previous studies have shown that tenocytes undergo apoptosis in response to hypoxia, oxidative stress, or excessive tensile load.[35,36,42] Therefore, using athletes' patellar tendon tissue with clinical and morphological features of tendinosis, we sought to determine the presence and extent of apoptosis in symptomatic but not ruptured tendons of young, active athletes, using antibodies against activated caspase-3 and fragmented DNA.

METHODS

Patient Groups

The patient group (n = 23) included athletes from different sports who were included in a prospective randomized trial comparing surgery with eccentric training.[2] The following diagnostic criteria were used for patellar tendinopathy: history of exercise-related pain in the proximal patellar tendon or the patellar insertion and distinct tenderness to palpation corresponding to the painful area.[5] To be included in the study, patients had a clinical diagnosis of jumper's knee grade IIIB, that is, pain during and after activity and inability to participate in sports at the same level as before the injury.[26] In addition, to ensure that the biopsy specimens were taken from the tendinopathic area, a thickening and signal changes corresponding to the painful area on MRI were required. Finally, patients had to have experienced symptoms for a minimum of 3 months and be willing to undergo surgery.

Each patient went through a standardized interview, and the information requested from each athlete included age, height, weight, and number of years participating in organized athletic training. Patients were asked to report the number of training hours per week during the competition season (sport-specific training, weight training, jump training, and other types of training). To assess the severity of the condition, the athletes with diagnosed current patellar tendinopathy also self-recorded their symptoms and level of sports function using the Victorian Institute of Sport Assessment (VISA) questionnaire.[41] This brief questionnaire assesses symptoms, function, and the ability to play sports.[41] The maximal VISA score for an asymptomatic, fully performing individual is 100 points, and the theoretical minimum is 0.[41] The VISA questionnaire is a reliable and valid measure of symptoms in patients with patellar tendinopathy.[41]

The control group (n = 11) was selected from patients treated with marrow nailing for tibia fractures from low-energy trauma. These patients had no current or previous knee complaints indicative of patellar tendinopathy. Subjects in both groups had to be at least 18 years old (to ensure that the epiphyses were closed) and able to understand oral and written Norwegian.

Exclusion criteria in both groups were previous surgical treatment in or around the same knee, corticosteroid injections in or around the same knee, serious traumatic injury affecting the same knee, and any rheumatic or degenerative knee condition. The study was approved by the Regional Committee for Research Ethics, participation was voluntary, and written consent was obtained.

Surgical Technique

The surgical exposure was identical in the 2 groups, with a 5-cm longitudinal midline or lateral parapatellar incision, splitting of the paratenon, and exposure of the patellar ligament. The paratenon was split longitudinally; any pathologic paratenon tissue was removed, and the tendon was fully exposed. In both groups, biopsy specimens were taken from the proximal bone-ligament junction, and the tendon tissue was excised using a full-thickness wedge-shaped incision, being widest at the patellar pole and narrowing distally. In the patient group, all abnormal tissue was removed. If clearly abnormal tissue was not seen macroscopically, the excision was based on MRI signal changes. The lesion was located on the MRI scan, and the corresponding area was debrided during surgery. Typically, a wedge with a proximal base 1 cm wide and extending to an apex 2 to 3 cm distal from the patellar pole was removed. All biopsy specimens were taken from the proximal patellar tendon.

In the control group, biopsy samples were taken with a width of at least 5 mm and a length of at least 20 mm from the middle portion of the ligament starting at the bone-ligament junction. A suture was passed through the proximal end of the tendon to allow its identification during subsequent processing.

Biopsy Procedure

The handling of the biopsy specimens was identical in the 2 groups. Immediately after the surgical procedure, the specimens were transferred to Zamboni's solvent.[46] They were stored in this solution for 4 to 24 hours and then washed in 0.1 M phosphate-buffered NaCL, pH 7.2, with 15% sucrose (weight/volume) (PBS) and 0.1% natriumazide. This washing was done until the yellow color from the Zamboni solution could no longer be seen in the phosphate-buffered saline (PBS). The specimens were then stored in PBS at 4°C

for a minimum of 48 hours, after which they were embedded in paraffin.

Light Microscopic Appearance

Sections of 5-µm were routinely stained for hematoxylin and eosin (general morphologic characteristics) and Alcian Blue (sulphated glycosaminoglycans) and viewed at 100 to 630 magnification on a Zeiss Axioplan (Carl Zeiss Inc. Thornwood, NY) upright microscope. Areas of adipose or peritendinous tissue were avoided during subsequent analysis.

Detection of Apoptosis and Assessment of Caspase Activation

Apoptosis was assessed using a monoclonal antibody against single-stranded DNA breaks (F7-26; Chemicon, Temecula, USA) as described previously,[36] as well as with a polyclonal antibody against the active (cleaved) form of caspase-3 (Asp 175; Cell Signaling, Danvers, Ma) and propidium iodide staining (Sigma-Aldritch, St Louis, Mo) for nuclear shape. Of these methods, the cleaved caspase-3 antibody yielded the most specific and reproducible labeling of apoptotic cells in tonsil tissue (serving as a positive control) and was thus used for systematic quantification. The sections were cleared, quenched in 3% hydrogen peroxide, incubated in protein-free block for 15 min, then left overnight with the antibody diluted 1:50 in 0.1% bovine serum albumin in tris buffered saline (TBS). Slides were then sequentially exposed in a dark, moist chamber to horseradish peroxidase-conjugated goat-antirabbit (1:100, 30 min), fluorescyl-tyramide amplification reagent (DAKO Diagnostics, Glostrup, Denmark), antifluroescein-horseradish peroxidase, and finally 3,3´-diamino-benzidine (Vector Laboratories, Burlingame, USA) for 5 minutes (’), with 3 × 5’ washes in TBS between each step. Identically fixed and processed tonsil tissue, with or without the primary antibody, was used as positive or negative control, respectively.

Image Analysis

The identity of slides was masked with black tape. Using a 40× objective lens, the tissue section was illuminated with halogen or fluorescent light (488 nm wavelength), and respective areas of positive F7-26 or propidium iodide staining were captured at 1392 × 1045 pixels with a digital camera (Retiga Exi 1394, Qimaging Corp, Burnaby, Canada). For quantitation of apoptosis, 15 random areas (0.30 mm^2 each) from the proximal region were digitized. Cells were considered positive only if the labeling was intense and suggestive of apoptotic morphology.[30] A standard exposure time (50 ms) was used, and the contrast was not digitally adjusted.

Data Analysis

For quantitation of apoptosis, the following variables were compared using caspase-3 labeled tissue sections: total number of positive cells in all areas (x), total number of cells counted (y), Apoptotic Index ($x \div y * 100\%$), number of positive fields, and average number of positive cells per field. Results are presented as means with standard deviations (SD) unless otherwise noted. Comparisons between normal and tendinosis tissue were performed using the t test for independent samples (SPSS 13.0, SPSS Inc, Chicago, Ill, USA). Levene’s test for equality of variances was used with significance predetermined at $P = .05$, and the data were visually inspected to determine their normality.

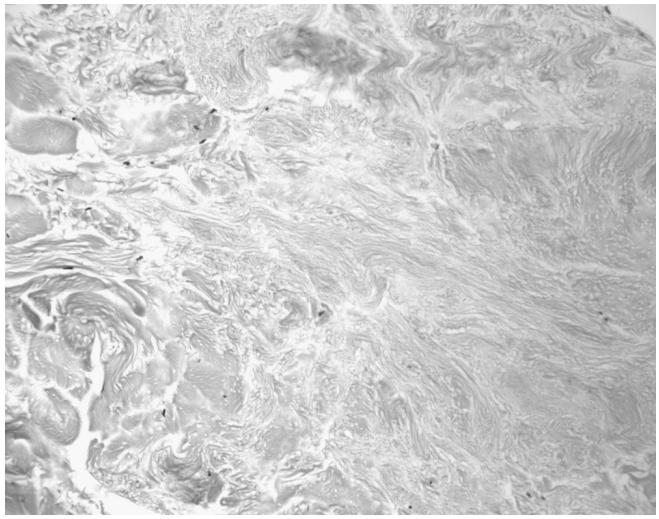

Figure 1. Patellar tendinosis specimen stained with hematoxylin & eosin, demonstrating a typical area of hypocellularity in association with collagen degeneration (100×). Note large area of absent cells in upper right.

RESULTS

Patient Characteristics

The mean age in the patient group was 30 years (24-34 years, n = 23) and in the control group, 29 years (19-43 years, n = 11). In the patient group, the mean number of years participating in organized training was 17 (10-28 years), and the mean number of total training hours per week was 14 (6-24 hours). The mean VISA score was 42 (15-65), and the mean duration of symptoms was 36 months (5-120 months).

Light Microscopic Appearance

Biopsy specimens from patients with a clinical history of tendon pain consistently revealed tendinosis, including areas of hypocellularity (Figure 1), as well as neovascularization with vessel wall thickening and collagen disarray and degeneration. Increased amounts of glycosaminoglycan were localized to areas of fibrocartilagenous metaplasia or to the tunica media of the vessel and perivascular regions. Inflammatory cells were virtually absent. Biopsy specimens from control tendons did not demonstrate any increase in vessel number or glycosaminoglycan content.

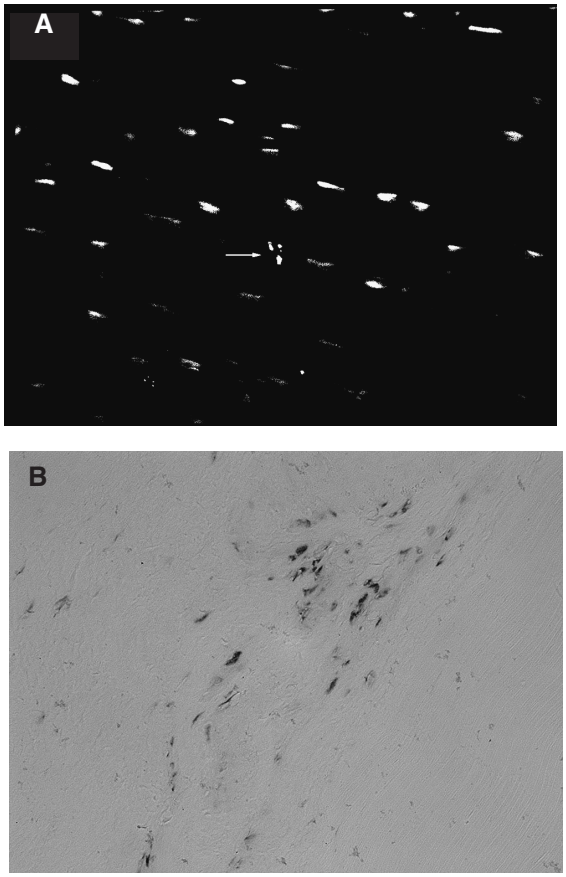

Figure 2. Demonstration of apoptosis in patellar tendinosis. A) Propidium iodide stain; arrow indicates fragmented nuclear shape (400×). B) F7-26 antibody demonstrating a cluster of apoptotic cells (200×).

Apoptosis in Normal and Overused Tendons

Apoptotic tenocytes were identified using all 3 methods (F7-26, propidium iodide, caspase-3) both in normal and pathological tendon, and each method showed that apoptosis represented a small minority of total cell counts (<1%). Apoptosis was predominantly found in fibroblast-like cells in the tendon proper (Figure 2A). Clusters of 5 to 10 apoptotic cells were observed in the tendinosis samples, compared with scattered or no cells in the controls (Figure 2B). Intense labeling with the caspase-3 antibody corresponded with nuclear fragmentation and condensation (Figure 3C). Faint cytoplasmic staining was sometimes observed and was interpreted as nonspecific (Figure 3D).

The number of apoptotic cells per unit area (4.5 mm^2) was 0.91 ± 0.81 in tendinosis samples and 0.21 ± 0.21 in controls (P = .026). There were more areas with apoptotic cells in the tendinosis tissue (3.7 ± 0.20 vs 1.9 ± 1.2, P = .006). In addition, fields from tendinosis patients that displayed positive staining had more apoptotic cells than positive fields from controls (3.1 ± 2.2 vs 1.5 ± 0.89, P = .006). Although the tendinosis samples displayed increased numbers of fibroblastic cells (162.5 ± 100 nuclei/mm^2 vs 98.9 ± 50 nuclei/mm^2, P = .021), the apoptotic index was higher (0.42 ± 0.38 % vs 0.17 ± 0.16 %, P = .014).

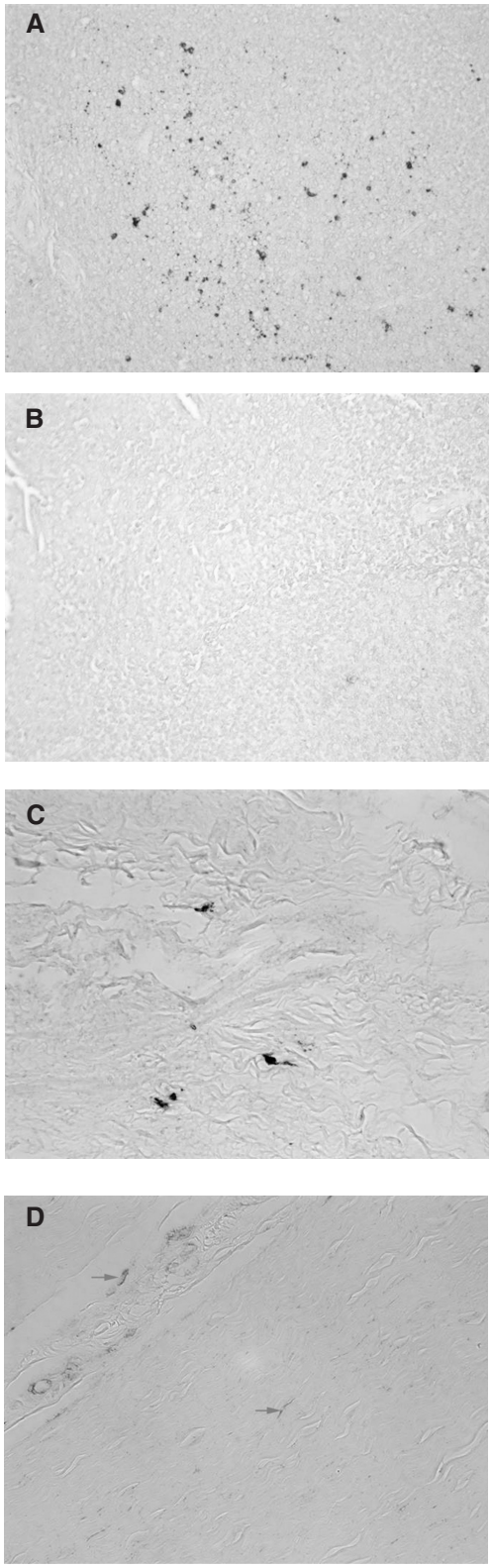

Figure 3. Demonstration of caspase activation in Bouin's fixed tissue. A) Positive staining for cleaved caspase-3 antibody coincides with apoptotic morphology in human tonsil. B) Omission of primary antibody yields no staining (100×). C) Intense labeling of tenocytes with fragmented morphology (200×). D) Arrows indicate background staining around vessels using the same conditions (200×).

DISCUSSION

The main findings in the present study were a significantly higher number of apoptotic cells per unit area and a significantly higher apoptotic index in biopsy specimens from the patellar tendons in patients with patellar tendinopathy compared with controls. Apoptotic tenocytes were identified using 3 methods: F7-26, propidium iodide, and caspase-3. The caspases are members of a family of cysteine proteases with a sequential activation and amplification system eventually causing apoptosis.[33] Since caspase-3 is one of the terminal proteins in the caspase activation system,[6,39] this finding denotes increased apoptotic activity in the patellar tendon in patients with patellar tendinopathy compared with controls.

To our knowledge, only 1 previous study has reported excessive apoptosis in the painful, nonruptured tendon.[40] That study used TUNEL staining, as well as the F7-26 antibody, to reveal apoptosis in the watershed area of the supraspinatus tendon with impingement. We note that apoptosis has also been seen in more severe tendon injuries, for example, tendon rupture.[43] How early in the pathogenesis of tendinosis apoptosis arises remains an important question.

The link between mechanical loading conditions and the pathophysiological response in tendinosis/tendinopathy is obscure, and currently there is insufficient evidence to provide a direct explanation for the possible connection between the loading pattern and the in vivo pathological response.[36] We have shown in case control[27] and cohort[28] studies that volleyball players with jumper's knee have better jumping ability and power generation than players who do not report symptoms from their tendons, presumably because they subject their knee extensors to higher loads when jumping and landing. Also, prevalence is higher in sports that require frequent jumping[25] and among athletes who train more.[16] Thus, there is reason to believe that there is a connection between the tendon-loading pattern and the pathologic changes within the tendon substance. In a study by Yuan et al,[43] excessive apoptosis was observed at the edge of torn rotator cuff tendons in elderly patients compared with controls. This has led to the proposal that tendinosis may begin as a degenerative process involving tenocyte death.[44] In support of this model, Skutek et al[39] suggested that mechanical stretching of tendon fibroblasts activates cell signaling pathways leading to apoptosis. However, once ruptured, the supraspinatus tendon would likely not receive excessive tensile loads, therefore other mechanisms such as oxidative stress, hypoxia, or remodelling may predominate in later stages. In another study, Barkhausen et al[3] found that different repetitive cyclic longitudinal stress patterns resulted in different cellular reactions depending on the strength of the applied stress. Repetitive stress applied during 1 day stimulated both proliferation and apoptosis.[3] In the current study, the number of tenocytes was increased overall, but there were also discrete areas of apoptosis and hypocellularity, suggesting that death and proliferation may be occurring simultaneously in response to repetitive loading, similar to the finding by Barkhausen et al.[3]

To successfully identify and quantify apoptotic cells in fixed tendon tissue, we used a well-characterized antibody recognizing active caspase-3, a key enzyme in the final common apoptotic pathway. This method resulted in specific labeling of cells with fragmented and condensed nuclei (Figure 3), which were found to compose <1% of the cell population in both patients and controls. This contrasts with a prior study of the patellar tendon[9] that reported surprisingly high rates of apoptosis in healthy controls (35% in rounded tenocytes and 26% in elongated tenocytes). It is not entirely clear why this discrepancy exists, but it likely relates to the use of the TUNEL technique, which has been criticized as generating many false-positive results.[24] Thus, the current paper presents a revised evaluation of the extent of tenocyte apoptosis in normal and painful patellar tendon.

A methodological limitation that must be considered when interpreting the results is that the diagnosis was based on clinical examination combined with MRI findings compatible with tendinosis. This means that to be recorded as having current symptoms of tendinopathy, the athlete had to report a painful tendon during athletic activity with corresponding palpation tenderness. It may be argued that this definition is nonspecific, since we do not know for certain that the tendon was the source of the pain in all cases. For instance, we could not rule out cases with referred pain, principally from the distal aspects of the articular surface of the patella. In fact, a number of studies have shown that the correlation between clinical findings and ultrasound[13,19,22,28,31] or MR examinations[7,14,22] is low, and even that symptoms and tendon changes come and go independently.[12,13] A significant number of athletes have or develop visible tendon changes without symptoms of jumper's knee, and some have significant pain without detectable tendon changes.[12,27] However, a diagnostic procedure based on MRI findings combined with a typical history and clinical findings is the most precise diagnosis of patellar tendinopathy currently in use. All athletes in the patient group had MRI findings localized to the proximal part of the patellar ligament, corresponding to the area where the biopsy samples were taken from. Thus, we would argue that the current diagnostic procedure is valid with regard to diagnostic precision and biopsy location. This is supported by the fact that the patients had an average symptom duration of 3 years and a VISA score of 42, which indicates a high level of pain and a significantly disabled patient group with chronic and severe complaints of patellar tendinopathy.

Our study contributes a novel insight toward understanding the pathologic changes associated with tendinosis, namely, that there is evidence of increased apoptosis in association with degenerate, nonruptured tendon compared with controls. However, there remain several limitations that must temper conclusions from our study. First, our cross-sectional study sheds no light on whether apoptosis preceded or followed the development of tendinosis. Second, our data were obtained in young athletes with chronic patellar tendinosis; we may not extend our conclusions beyond this population as yet. These limitations encourage future studies in other symptomatic or asymptomatic

tendons with early tendinosis, but it is a challenge to obtain such biopsy samples.

CONCLUSION

Our study demonstrates an increase in the extent of tendon cell apoptosis in athletes with patellar tendinopathy. The role of apoptosis within the broader framework and time course of tendon overuse injury remains to be established.

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