ACHILLES TENDON RUPTURES

PREDICTORS; FUNCTIONAL AND ECONOMIC IMPACT

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“Throughout the centuries there were men who took first steps, down new roads, armed with nothing but their own vision”.

Ayn Rand

TABLE OF CONTENTS

1

ABSTRACT

“To my children Otto and Ilse”

Acute Achilles tendon rupture is a common injury, which leads to significant morbidity in patients. Many patients never recover their full function even after long rehabilitation, whereas others make a good recovery. The factors behind this are unknown. The optimal treatment strategy, whether or not to treat surgically, is still controversial. This thesis consists of six studies with the overall aim of finding predictors of outcome, examining the long-term follow-up of re-ruptures and comparing the cost efficiency of two different management strategies.

Study I is a cohort study of 45 patients who underwent acute ultrasonography within 72 hours of the index injury. They were randomly allocated to either surgical or non-surgical treatment. Three out of four (75%) patients with a diastasis of more than 10 mm treated non-surgically sustained a re-rupture and these were the only re-ruptures in the study group. The patients with a diastasis of more than five mm displayed poorer heel-rise function and patient-reported outcome if treated non-surgically.

Study II is a cross-sectional observational cohort study comprising 256 prospectively randomised patients. At two weeks post-operatively, patients underwent a micro-dialysis investigation and six metabolites were collected. Patients were followed up at three, six and 12 months and the duration of surgery was examined. The results showed that glycerol and glutamate were higher with a longer duration of surgery. Interestingly, a longer duration of surgery was correlated with an improved clinical and functional outcome.

Study III is a long-term follow-up of patients with an Achilles tendon re-rupture, where validated outcome measurements were used to assess lower extremity function and symptoms. Twenty patients with a mean (SD) follow-up of 50.9 (38.1) months were included. This cohort was compared with patients (n=81) treated for primary ruptures. The injured side was significantly worse compared with the healthy side in terms of heel-rise tests. The most interesting finding in this study was that patients treated for a re-rupture reported a poorer patient-reported outcome compared with those treated for primary ruptures.

Study IV is a health-economic evaluation comparing the cost-effectiveness of surgical and non-surgical treatments. The data were collected prospectively from a randomised controlled trial comprising 100 patients. This study showed that the cost per quality-adjusted life year (QALY) gained is € 45,855 and that surgical treatment is 57% likely to be cost efficient at a willingness to pay per QALY of € 50,000.

Study V is a mapping study that develops an algorithm, which converts the Achilles tendon total rupture score (ATRS) to the European Quality of Life-5 dimensions Questionnaire (EQ-5D), which enables detailed health-economic studies related to Achilles tendon injuries. It concludes that the algorithm has a high goodness of fit and can be used in future studies. Study VI comprised 391 patients from five different randomised controlled trials predicting functional and patient-reported outcome one year after an acute Achilles tendon rupture. This study revealed that older age is a predictor of poorer outcome and that surgically treated patients have a tendency towards superior recovery in terms of heel-rise height.

Taken together, this thesis shows that ultrasonography could be potentially useful in predicting the risk of re-rupture and outcome in acute Achilles tendon rupture. It also demonstrates that a longer duration of surgery leads to the upregulation of healing metabolites. Patients who have sustained a re-rupture have long-term deficits in terms of function and a poorer patient-reported outcome than those with primary ruptures. Moreover, it provides the first cost-effectiveness analysis in this field of research and develops an algorithm for future health-economic studies. Finally, it concludes that older age is a strong predictor of poorer heel-rise height at one year.

KEYWORDS:

Achilles tendon rupture, re-rupture, predictors of outcome, health economics, Achilles tendon Total Rupture Score (ATRS)

2

SAMMANFATTNING PÅ SVENSKA

Hälseneruptur är en vanlig skada som ofta leder till bestående morbiditet. Många patienter återfår aldrig den funktion som de hade innan skadan, trots lång rehabilitering medan andra återfår normal funktion. Vilka faktorer som påverkar detta är okänt. Den optimala behandlingen av den akuta hälseneruptúren, d.v.s. operativ alternativt icke-operativ behandling är fortfarande omdebatterad. Denna avhandling består av sex studier med övergripande mål att undersöka vad som leder till bättre respektive sämre utfall, långtidsuppföljning av re-rupturer samt att jämföra kostnadseffektivitet mellan operativ och icke-operativ behandling.

Studie I är en kohortstudie som inkluderar 45 patienter, vilka genomgick akut ultraljudsundersökning inom 72 timmar från skadetillfället. De randomiserades till antingen operativ eller icke-operativ behandling. Tre av fyra (75%) patienter med en diastas på över 10 mm, som behandlades icke-operativt, ådrog sig en re-ruptur. Inga ytterligare re-rupturer rapporterades i studien. Patienter med en diastas på mer än fem mm som behandlades icke-operativt visade dessutom sämre funktion avseende tåhävningstester och patientrapporterade utfallsmått vid uppföljning.

Studie II är en prospektiv tvärsnittsstudie på en grupp av 256 patienter där samtliga opererades. Två veckor efter operation genomgick patienterna mikrodialysundersökning och sex metaboliter samlades in. Patienterna följdes sedan upp tre, sex och 12 månader efter operation och deras operationstider studerades. Resultaten visade att glycerol och glutamat var högre vid längre operationstid. Förvånande nog demonstrerade det sig att längre operationstid korrelerade med bättre funktionellt utfall.

Studie III är en långtidsuppföljning av patienter som ådragit sig en re-ruptur. Tjugo patienter med re-ruptur med en genomsnittlig uppföljningstid på 50.9 (38.1) månader inkluderades. Validerade utfallsmått användes för att studera nedre extremitetsfunktionen. Dessa patienter jämfördes med patienter med primära rupturer. Den skadade sidan visade sig vara signifikant sämre jämfört med den friska avseende tåhävningstester. Det viktigaste fyndet var att patienter med re-ruptur hade signifikant sämre patientrapporterade besvär jämfört med de med primära rupturer, men inte i funktion.

Studie IV är en hälsoekonomisk studie, som jämför kostnadseffektiviteten mellan operativ och icke-operativ behandling hos 100 patienter som studerats prospektivt. Studien visade att kostnaden per vunnet levnadsår är 45,855 euro och att operativ behandling är med 57% sannolikhet mer kostnadseffektiv om man är villig att betala 50,000 euro för ett vunnet levnadsår.

Studie V utvecklar en algoritm, som konverterar Achilles tendon Total Rupture Score (ATRS) till European Quality of Life-5 dimensions frågeformulär (EQ-5D). Detta gör det möjligt att utföra fördjupade hälsoekonomiska studier inom hälseneområdet där ARTS används som utfallsmått. Studien visade att algoritmen har en mycket hög ”goodness of fit” och kan användas vid framtida studier.

Studie VI, som är den sista studien i avhandlingen omfattar 391 patienter från 5 olika randomiserade studier och predikterar funktionella och patient-rapporterade utfallsmått 1 år efter en akut hälseneruptur. Studien visar att högre ålder är en prediktor för sämre utfall och att operativt behandlade patienter har en tendens till bättre återhämtning av tåhävningshöjd.

Sammanfattningsvis visar avhandlingen att akut ultraljud kan potentiellt vara värdefullt för att prediktera re-ruptur och funktionellt utfall efter en akut hälseneruptur och därigenom styra behandlingsval, samt eventuellt fungera som stöd vid beslutsfattandet för operativ behandling. Den visar att längre operationstid är relaterad till uppreglering av metaboliter samt att patienter som ådrar sig re-rupterer har sämre patientrapporterade utfall jämfört med patienter med primära rupturer. Avhandlingen innehåller även den första hälsoekonomiska analysen inom detta forskningsfält och utvecklar en algoritm för framtida hälsoekonomiska studier. Slutligen kunde det visas att högre ålder var en stark prediktor för sämre resultat ett år efter en akut hälseneruptur.

3
LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. **Acute ultrasonography investigation to predict reruptures and outcomes in patients with an Achilles tendon rupture.**
Westin O, Nilsson-Helander K, Grävare Silbernagel K, Möller M, Kälebo P, Karlsson J.
Orthopedic Journal of Sports Medicine. 2016 Oct 14;4(10), 2325967116667920

II. **Longer duration of operative time enhances healing metabolites and improves patient outcome after Achilles tendon rupture surgery.**
Svedman S, Westin O, Aufwerber S, Edman G, Nilsson-Helander K, Carmont M, Karlsson J, Ackerman PW.
Knee Surgery Sports Traumatology Arthroscopy. 2018 Jul;26(7):2011-2020

III. **Patients with an Achilles tendon re-rupture have long-term functional deficits and worse patient-reported outcome than primary ruptures.**
Westin O, Nilsson-Helander K, Grävare Silbernagel K, Samuelsson K, Brorsson A, Karlsson J.
Knee Surgery Sports Traumatology Arthroscopy. 2018 Oct;26(10):3063-3072.

IV. **Cost-effectiveness analysis of surgical versus non-surgical management of acute Achilles tendon ruptures.**
Westin O, Svensson M, Nilsson-Helander K, Samuelsson K, Grävare Silbernagel K, Olsson N, Karlsson J, Hansson-Olofsson E.
Knee Surgery Sports Traumatology Arthroscopy. 2018 Oct;26(10):3074-3082.

V. **Mapping functions in health-related quality of life: mapping from the Achilles Tendon Rupture Score to the EQ-5D.**
Hua A-Y, Westin O, Hamrin Senorski E, Svantesson E, Grassi A, Zaffagnini S, Samuelsson K, Svensson M.
Knee Surgery Sports Traumatology Arthroscopy. 2018 Oct;26(10):3083-3088.

VI. **Older age predicts worse outcome one year after an acute Achilles tendon rupture: A prognostic multicenter study on 391 patients**
Westin O, Svedman S, Hamrin-Senorski E, Svantesson E, Nilsson-Helander K, Karlsson J, Ackerman PW, Samuelsson K.
Orthopedic Journal of Sports Medicine (accepted for publication)

Book chapters not included in the thesis:

Minimally Invasive Lengthening of the Achilles Tendon
Olof Westin, Jonathan Reading, Michael R. Carmont, Jon Karlsson.
Minimally-Invasive Lengthening of the Achilles Tendon. 2017. Page 113-118
In: Thermann H. et al. (eds) The Achilles Tendon. Springer, Berlin, Heidelberg

4

ABBREVIATIONS

ATR	Achilles tendon rupture
ATRS	Achilles tendon total rupture score
BMI	Body mass index
CI	Confidence interval
DOT	Duration of operation time
Drop CMJ	Drop counter-movement jump
EQ-5D	EuroQol, a generic health-related quality of life score
FAOS	Foot and ankle outcome score
ICC	Intra-class correlation coefficient
ICER	Incremental cost-effectiveness ratio
LSI	Limb symmetry index
MDC	Minimal detectable change
MRI	Magnetic resonance imaging
PAS	Physical activity scale
PROMs	Patient-reported outcome measurements
QALY	Quality-adjusted life years
RCT	Randomised control trial
SD	Standard deviation
US	Ultrasonography

5

DEFINITIONS

Body mass index (BMI)	Weight(kg)/height(m^2)
Hopping	A continuous rhythmical jump, similar to skipping with a rope
Hopping quotient	The same as plyometric quotient. Flight time divided by contact time
Incidence	The number of new cases of a condition or injury that develops during a specific period of time, such as a year
LSI	Limb symmetry index. The LSI is defined as the ratio of the involved limb score and the uninvolved limb score expressed in per cent (involved/uninvolved x100 = LSI)
Negative predictive value	The proportion of individuals with a negative test result that do not have a specific condition
Non-parametric statistics	A statistical method where the data are not required to fit a normal distribution
Parametric statistics	A statistical method that relies on assumptions of a normal distribution
Positive predictive value	The proportion of individuals with a positive test result that have a specific condition
Power	Power is the product of force and velocity expressed as watts (W) or Newton-meters/second (Nm/s)
Predictor	The independent variable used to predict or explain the outcome (dependent) variables
Quality adjusted life years	Generic measure of disease burden, including both the quality and the quantity of life lived. It is used in economic evaluation to assess the value for money of medical interventions. One QALY equates to one year in perfect health.

Sensitivity	The proportion of individuals with a condition that has a negative result in a specific test
Specificity	The proportion of individuals without a condition that has a negative test
Standing heel rise	An exercise in which the subject performs a plantar flexion while standing
Work	The product of a constant force and the distance the object is moved in the direction of that force. The SI unit is joules (J).

6
INTRODUCTION

Figure I. The Greek hero with an arrow in his Achilles tendon

6.1. THE ACHILLES TENDON

The history of the Achilles tendon dates all the way back to the first century AD, when the Greek poet Statius wrote a poem about the invulnerable warrior Achilles. According to the legend, Achilles was a great warrior and leader in the Trojan War. His father, Peleus, was king of the Myrmidons and his mother was the sea nymph, Nereid Thetis. Achilles became immortal in every part of his body apart from his heel, as his mother held him by the heel as she dipped him as an infant in the River Styx that forms the boundary between the earth and the underworld. His immortal mother prophesied that he would either live a long and uneventful life or he would die young as a hero. Achilles chose the latter. The most notable triumph for Achilles was when he managed to kill Hector, the Trojan warlord. Achilles was killed by Paris who shot a poisoned arrow and hit him in his vulnerable heel. This myth is the foundation of the statement "Achilles heel", which is the point of weakness in an otherwise robust construction.

In medicine, the first description of a closed Achilles tendon rupture is attributed to the French barber surgeon, Ambroise Paré, in 1575 and is reported in the literature in 1633. However, he did not make the connection with the Greek hero; this was done at a later stage and the origin is disputed. Many attribute it to the Flemish surgeon and author, Philip Verheyen. In his youth, Verheyen studied to become a priest and during this time he became ill and was forced to amputate his left leg. With one leg, he was no longer able to join the clergy and had to settle for medicine and he described the Achilles tendon rupture in 1693[125].

Gothenburg has a strong history of Achilles tendon research, with the first ever randomised controlled trial (RCT) studying surgical versus non-surgical treatment published in 1981 by Nistor[130]. This has been followed by a further three high-quality RCTs[120, 127, 138], which have improved our understanding of how to treat this injury and laid the foundation for this thesis.

Since the Achilles tendon is such an important structure and ruptures are common, a Pubmed search for "Achilles tendon rupture" yields more than 10,000 articles to date. Despite being extensively researched, there is still no consensus on the optimal treatment regimen, i.e. surgical or non-surgical treatment. Recently, the focus has shifted towards individualised treatment and, in order to achieve a treatment protocol of this kind, we need a better understanding of the factors that affect the patient-related outcomes, both in terms of patient characteristics and from an economic perspective.

6.1.2. ANATOMY

The Achilles tendon is the largest and most powerful tendon in the human body[38]. It is formed by the soleus and gastrocnemius muscles and is located in the posterior superficial compartment of the leg. The gastrocnemius muscle has a fusiform shape and two heads. Medially, it arises from the popliteal surface of the femur, posterior to the medial supracondylar line and the adductor tubercle. Laterally, the head is shorter and originates from the lateral femoral condyle. It contains a large number of "fast" white, type II fibres, which make it important in explosive events such as jumping. As it crosses the knee joint, it not only performs supination and plantar flexion of the ankle joint, it also flexes the knee. In contrast, the soleus muscle, which originates from the middle third of the medial border of the tibia, does not cross the knee joint. It lies deep to the gastrocnemius muscle and is a large flat muscle containing mainly "slow" red, type I fibres that are important for maintaining posture[38]. Together, these two are often referred to as the triceps surae and they each make up roughly 50% of the tendon[36]. Lastly, there is a third muscle, called the plantaris muscle, which is absent in approximately 8% of the population[167]. It is a small muscle which originates from the popliteal fossa of the femur. The average length of the Achilles tendon is 15 cm (range 11-26 cm), the mean width is 6.8 cm (4.5-8.6 cm) at its origin and this gradually decreases to the midsection, where the average width is 1.8 cm (1.2-2.6 cm)[40].

As is well known, the Achilles tendon is important for athletic performance, such as running and jumping. The reason it can produce such a forceful elastic recoil and elongation is due to the spiralling of the tendon[107] (Figure II). It spirals 90 degrees and, in doing so, allows for elongation and elastic recoil, but it also produces an area of concentrated stress in the midportion[5]. The degree of spiralling depends on the position of the fusion between the two muscles. More distal fusion increases the rotation. The insertion of the tendon in the calcaneus is crescent shaped. A bursa named the retrocalcaneal bursa is located between the tendon and the calcaneus and is claimed to reduce friction during motion[8, 52].

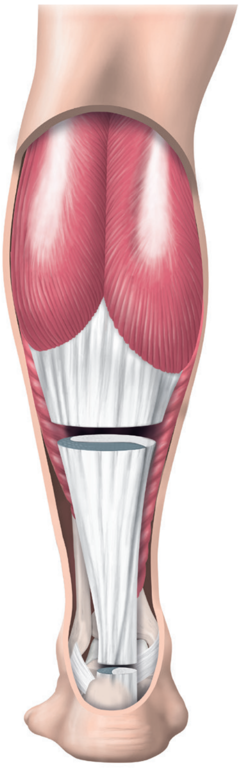


Figure II. The Achilles tendon anatomy. This figure shows the rotation of the tendon, between the muscle and insertion to the calcaneus

6.1.3. TENDON STRUCTURE

The structure of the tendon is illustrated in figure III. The smallest units, collagen fibrils, are organised into fibres, which are further organised into primary, secondary and tertiary fibre bundles[76, 134]. The strength of the Achilles tendon, which enables it to sustain forces up to 12 times the weight of the body during running, is a result of its design and its high density of the strong type I collagen. Like all tendons, the Achilles tendon is formed by a combination of collagen and elastin embedded in a proteoglycan-water matrix. As previously stated, type I collagen is dominant, with between 60-85%, plus 0-10% type III collagen and 1-2% elastin[134, 135]. The Achilles tendon is covered by several layers of connective tissue (paratenon, epitenon, endotenon) and the neurovascular supply is located in the endotenon. Interestingly, after injury to the Achilles tendon, the proportion of the weaker type III collagen is increased, which might affect its tensile strength[140].

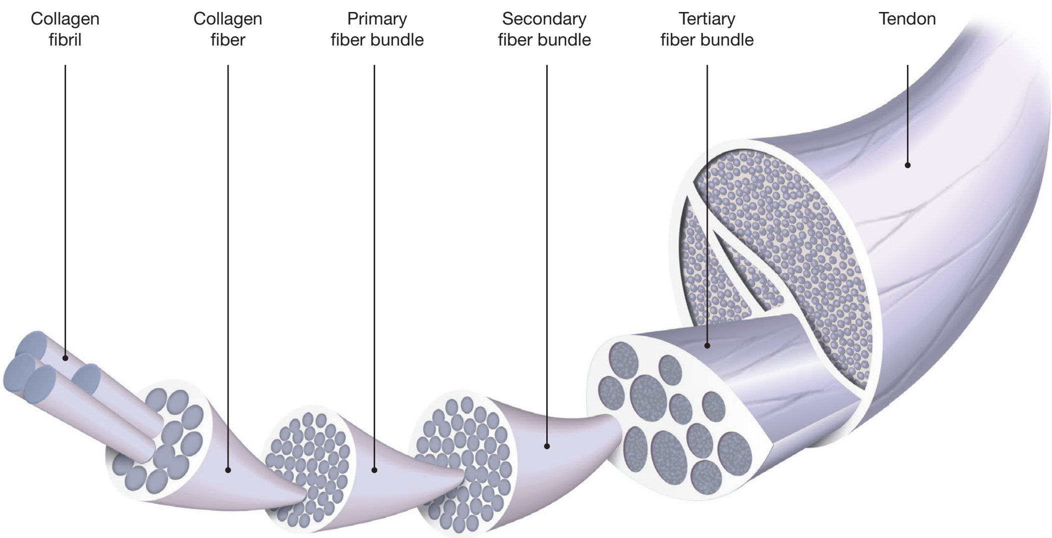


Figure III. *The organisation of the tendon structure from collagen fibrils to the entire tendon*

6.1.4. BIOMECHANICS OF THE TENDON

Tendons have viscoelastic properties similar to those of a spring and their function is to transmit force from muscle to bone[50, 112, 147]. When studying Achilles tendon biomechanics, it is important to note that it is not only the tendon itself that transmits the force but also the so-called muscle-tendon complex, which consists of the tendon as well as its muscle and aponeurosis which work as a unit[57]. Similar to spring, the Achilles tendon is able to store energy and release it at a later point in time. When jumping on one leg, 74% of the mechanical energy is stored and 16% of the total mechanical energy comes from the elastic recoil action of the Achilles tendon[98]. The concept of a force-length relationship in tendons has been studied in detail[49, 84, 114]. When force is applied to a tendon, it will lengthen and the effect is demonstrated in the stress-strain curve, see figure IV.

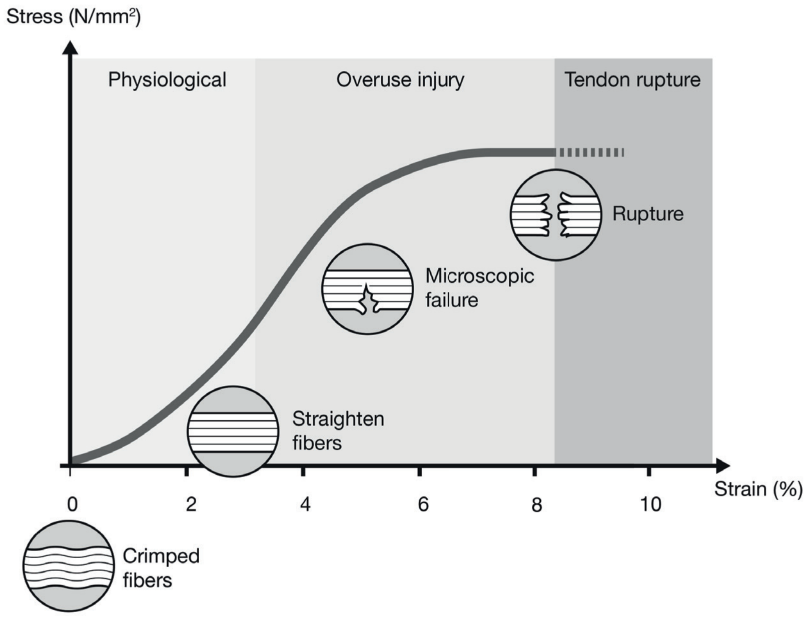


Figure IV. *Tendon stress-strain curve*

The stress that is placed on the tendon is calculated by dividing the force by the cross-sectional area of the tendon and this is reported as force per unit area; hence a thicker tendon is able to sustain a higher load than a thinner one. The tendon stress-strain curve has three different regions that reflect the change in strain (%) from the stress (n/mm^2) that is applied. The first is the physiological region, also known as the toe region of the curve, which is the non-linear part of the curve where the fibres are stretched out on mechanical loading, whereby no damage occurs. The second is the linear region, which is also known as Young's modulus. This represents the upper limit of physiological change in the tendon. The tendon cell deforms in linear fashion, so, if the strain is less than 4%, the tendon will return to its original length when the load is removed, but microscopic failure will occur above this level. Finally, there is the yield and failure region and the percentage of stress at which this occurs varies between studies[81, 111, 185]. Eight per cent is often quoted in the literature as the level at which macroscopic failure begins, figure IV[180]. During this phase, as the tendon fibres are stretched beyond their physiological capacity and the intra-molecular cross-linking between collagen fibres fails, this then leads to irreversible deformation[81].

6.1.5. CIRCULATION

The Achilles tendon is supplied by vessels of the anterior paratenon, which originates from the posterior tibial artery. This is supported by the peroneal artery through anastomoses. However, there is no connection to the anterior tibial artery[169]. Three main regions (proximal third, central third and distal third) of circulation have been identified and it has been hypothesised that the relative avascularity of the central third contributes to it being the most common rupture zone[4, 27]. However, other research disputes this and it varies depending on the method that is used to measure the blood flow[154, 169]. In a recent study by Praxitelous et al., a correlation was shown between good microcirculation in patients who have sustained an acute Achilles tendon rupture and improved patient-reported outcomes[143].

6.1.6. METABOLISM AND INNERVATION

Tendons have a low metabolism compared with skeletal muscle and use approximately 7.5 times less oxygen, which enables them to carry heavy loads and endure when under tension for prolonged periods[135]. Unfortunately, this slow metabolism makes tendon injury heal slowly. As tendons are living tissue, there is a continuous and ongoing process of collagen synthesis and degradation. Synthesis is highest during growth and after injury[135]. Degradation increases with age[180]. In this thesis, microdialysis is used to measure tendon metabolism two weeks following an acute Achilles tendon rupture. It is not well researched how metabolites such as, glutamate, glucose, lactate, pyruvate and glycerol, contribute to the healing of a ruptured Achilles tendon[82]. Ackermann et al.[1, 2] and Malloy et al.[122] were able to demonstrate that glutamate, which is involved in carbohydrate metabolism and is regarded as being involved in the tissue repair process, is present in the Achilles tendon during healing. All the above essential metabolites are needed for carbohydrate metabolism as well as for tissue repair and cell proliferation[69, 88]. Pyruvate and glycerol are basic structural elements that are of paramount importance for the energy metabolism required for wound healing. Glucose is the fuel that give cells energy and lactate was shown by Klein et al.[83] to enhance collagen synthesis at tendon repair sites. These essential metabolites have attracted increasing attention in research studies and may help us predict outcome in the future[174].

The main nerve supply to the Achilles tendon derives from the suralis nerve and the tibial nerve. It is estimated that the tendon receives its sensory innervation from adjacent, deep-lying nerves or from overlying superficial nerves[43].The paratenon is more richly innervated and contains receptors for proprioception called Pacinian corpuscles, which are important for good tendon function[134]. In figure V is an illustration of a ruptured tendon.

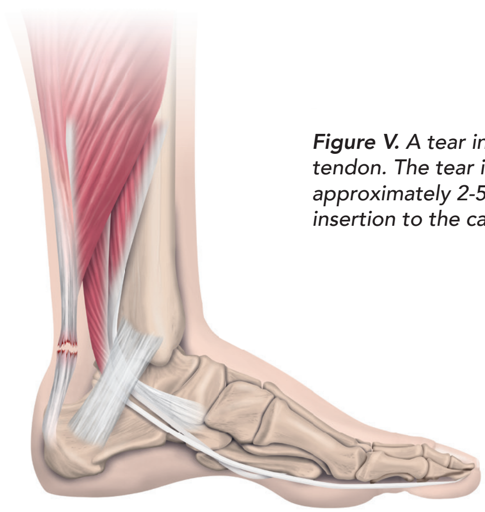


Figure V. *A tear in the Achilles tendon. The tear is usually located approximately 2-5 cm from the insertion to the calcaneus*

6.2. ACUTE ACHILLES TENDON RUPTURE

6.2.1. INCIDENCE

The incidence of Achilles tendon ruptures has been extensively studied[51, 68, 96, 97]. It has recently been reported to be 18 per 100,000 persons; however, it is well recognised that there is a regional variation and that the incidence is on the rise[51]. Lantto et al.[90] reported an annual increase of 2.4% over a 33-year period. The reason for this increase is most likely that people perform more sporting activities at a higher age and it has been demonstrated that ruptures in this population have increased. Achilles tendon rupture is more common in men than woman, with different ratios reported[68, 133, 177]. The ratio is generally quoted at 10:1[35]. Two age-related peaks in incidence have been reported[66]; one in the early 40s, often related to sporting activities, and one in the 60- to 65-year age group, often associated with lesser trauma[30, 110].

6.2.2. AETIOLOGY AND MECHANISM OF INJURY

The mechanism of an Achilles tendon rupture can be classified into three main categories, figure VI illustrates this:

Push-off with the weight-bearing foot while the knee is extended
Sudden unexpected powerful dorsiflexion of the foot
Forced dorsiflexion of the plantar flexed foot

The aetiology of an Achilles tendon rupture is complicated and multifactorial[30, 181]. Some researchers argue that degenerative changes occur in the tendon, which reduce its strength over time[28, 74, 109, 151], but this remains controversial[141]. This theory can help to explain the increase in incidence that has been correlated to the increasing participation in sporting activities in the middle-aged (around 40 years of age) group. At this age, degeneration has started and the tendon is unable to sustain the same forces. Also inflammatory disorders, such as rheumatoid arthritis, gout and lupus erythematosus, as well as chronic renal failure and diabete mellitus, have been shown to increase the risk of rupture[156, 184]. The role of corticosteroid injections as a risk factor has been much debated and the evidence is inconclusive[113, 126]. Another theory is that repeated microtrauma causes lasting weakness in the tendon, which might lead to rupture over time. Risk factors for ruptures and prevention are an area that warrants more extensive research.

Figure VI. *The mechanism of an Achilles tendon rupture*

6.3. CLINICAL ASSESSMENT OF AN ACHILLES TENDON RUPTURE

Patients often describe sustaining an Achilles tendon rupture as a sudden acute snap in their calf, as if someone had kicked them in the heel. This is followed by weakness and difficulty bearing weight[123]. Poor balance and altered gait are other well-reported clinical signs[123]. Sometimes, the clinical presentation can be somewhat difficult and it is reported that up to 25% of ruptures may be missed in the early phase by patients or physicians and they are often mistaken for an ankle sprain[9, 70].

Physical examination can prove to be a challenge to clinicians. Sometimes, the weakness that is suspected with a tendon rupture can be masked by the tibialis posterior, plantaris, flexor hallucis longus and flexor digitorum longus and peroneal muscles. Patients do not always experience pain on examination and this can be misleading. The tendon gap can also be difficult to palpate due to the surrounding swelling and adipose tissue that herniates into the gap. It is important to understand this and be able to examine an Achilles tendon clinically in order to reduce the incidence of missed diagnosis.

6.3.1. DIAGNOSTIC TESTS

Several specific tests have been described in the literature. The most frequently used is called Thompson's[172] test, it is also know as Simmond's[165] test or the calf-squeeze test[165], figure VII. This test is performed with the patient in a prone position with his/her ankles hanging off the examination table or with the knee flexed and the ankle free in the air. The examiner then squeezes the calf, which causes a deformation of the triceps surae muscle which then causes a shortening of the muscle that pulls the Achilles tendon away from the tibia[86]. The test is negative if plantar flexion occurs and this indicates that the tendon is intact. If there is no plantar flexion and/or a clear difference from the contralateral side, the test is positive. The sensitivity of the test has been reported as 0.96 and the specificity 0.93[105]. In 2014, Reiman et al.[145] performed a systematic review with a meta-analysis of different tests used to establish the diagnosis of Achilles tendon rupture. They found that the calf-squeeze test had a positive likelihood ratio of 13.51 and a negative likelihood ratio of 0.04. These data show that the test is excellent in ruling out an Achilles tendon rupture. The second clinical test that is important to perform is Matle's test, which is performed with the patient in a prone position with the knee flexed at 90 degrees. If an Achilles tendon rupture is present, the affected foot will fall back into a neutral position, while the contralateral healthy side remains in slight plantar flexion[116]. In the study by Maffulli et al.[105], Matle's test had a sensitivity of 0.88 and a positive predictive value of 0.92.

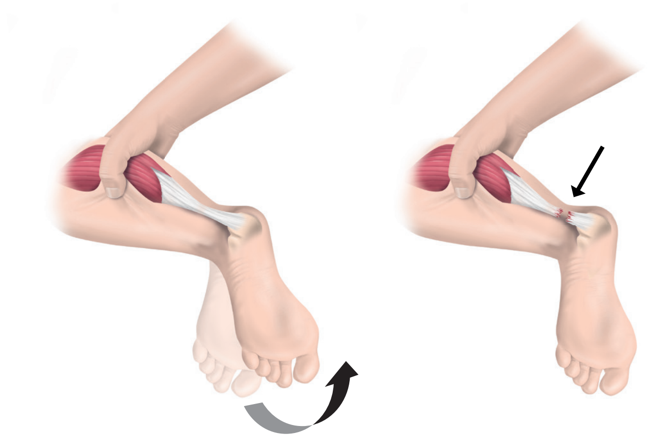


Figure VII. *Thompson's test. If there is no plantar flexion and/or a clear difference from the contralateral side, the test is positive*

6.4. ACUTE ULTRASONOGRAPHY

The higher incidence of re-ruptures in patients treated non-surgically may be due to incomplete healing, which could in turn be the result of a large initial gap between the tendon ends. Thermann and Zwipp[170] suggested that an initial diastasis of more than five mm would adversely affect functional outcome. Ultrasonography (US) in 25 degrees of plantar flexion was suggested to be able to identify those patients who were suitable for non-surgical treatment[6]. Ultrasound has been used as an imaging modality for the diagnosis and evaluation of injuries for more than 20 years[53]. However, acute Achilles tendon rupture is a clinical diagnosis in the first place, where the history of an audible snap and sudden pain combined with a palpable gap, as well as a positive Thompson's test and Malte's test, is sufficient to establish the diagnosis[105]. In patients with a typical history of trauma, a complete rupture can be assumed, as partial ruptures are uncommon[105]. Ultrasound has not been recommended as a means of establishing the diagnosis, as there is risk that the patient might not be treated correctly if the physician relies too heavily on US alone[106]. On the other hand, Kotnis et al.[85] used dynamic US as a selective criterion for determining whether patients should receive surgical or non-surgical treatment. According to these researchers, a gap of less than five mm was proposed as a limit for patients in whom non-surgical treatment could be recommended. However, to the best of our knowledge, this thesis presents the first prospective comparative study performed, using acute US to predict re-ruptures and correlate the US measurements to subjective and functional outcome. To our knowledge there is no previous literature that has evaluated whether there is a difference in terms of complications, symptoms and function in patients with differently sized diastases.

Question

Can the measurement of the tendon gap through ultrasonography help to determine whether a patient requires surgery in order to minimise the risk of re-rupture and improve the clinical outcome?

6.5. TREATMENT OF ACHILLES TENDON RUPTURES

The way in which Achilles tendon rupture should be managed can be divided into either surgical or non-surgical treatments. The question of which is superior has been studied in several randomised controlled trials and meta-analyses[11, 41, 64, 73, 79, 80, 100, 118, 166], but there is still no consensus on whether or not to operate. Over time, the pendulum has swung in both directions. It started in 1929, when Qenu published an article that declared that treatment should be surgery as soon as possible[144]. This was the management strategy of choice until the 1970s, when evidence started to appear indicating that it was not necessary to operate in order to heal the tendon[93, 94]. Two key publications have in recent time made non-surgical treatment more popular, both reporting a good outcome after non-surgical treatment with early accelerated rehabilitation[127, 183]. In 2013 Barfod et al.[10] performed a study and sent out questionnaires to 138 orthopaedic departments across Scandinavia. The authors found that 65% would favour the surgical treatment of active people under the age of 60 in Sweden. Non-surgical treatment is commonly performed using cast immobilisation for the first two weeks, followed by an orthosis for another six weeks, after which a gradual reduction in plantar flexion is started. Early weight-bearing is recommended. Surgical treatment can be sub-categorised into three main types: open repair, minimally invasive repair and percutaneous repair. Each has its own advantages and disadvantages.

OPEN REPAIR

This is the traditional way of surgically addressing an Achilles tendon rupture and is the technique that is used in this thesis. A surgical incision is made over the tendon and all the sutures are placed via that incision. The tendon is exposed in the wound and it allows for direct visualisation of the rupture and the repair. Compared with the other methods, more damage is done to the soft tissues. Both Nilsson-Helander et al.[127] and Olsson et al.[138] used this technique in their RCTs on which this thesis is based. It is worth noting that Olsson et al. reported 0% re-ruptures[138]. The obvious drawback to open repair is the risk of wound infection, adhesions and, in the worst-case scenario, wound breakdown[121]. Necrosis of the wound can be disastrous and lead to major reconstructive surgery and long rehabilitation[20].

MINIMALLY INVASIVE REPAIR/PERCUTANEOUS REPAIR

It is difficult to draw a clear distinction between a minimally invasive and a percutaneous repair, as the terminology has blended together over time. These repairs have the goal of suturing the tendon together with minimal trauma to the soft tissue. This can be done in numerous different ways as recently described in a thesis presented by Carmont[23]. As the incision is small, there is less risk of wound problems. This method is also cosmetically advantageous in comparison with open repair, but the main drawback is the increased risk of sural nerve injury.

NON-SURGICAL TREATMENT

Historically, methods of non-surgical treatment has included immobilization in a cast for three months followed by referral to a physiotherapist[120] There are several other established methods of non-surgical treatment including the use of bespoke braces[171] boots with wedges[71, 183] controlled ankle motion walkers[127] and conforming vacuum walkers with graduated ankle posture[67]. Recent meta-analyses have suggested re-rupture rates similar to those of surgical treatment, for non-surgical management when early weight-bearing and range of motion exercises are implemented[166].

In non-surgical management it is important to include a clinical examination after two weeks of cast immobilisation[46, 67]. If there is an abnormal resting posture to the ankle or a palpable gap is still present surgical repair should be recommended. Non-surgical treatment in the presence of greater than one cm diastasis of the tendon ends has been shown to lead to worse outcome[92]. Re-rupture rates in non-operative treatment may be minimized further by the prolonged wearing of braces for as much as 4 months during at risk activities[46, 67].

REHABILITATION

Rehabilitation following an Achilles tendon rupture is of great importance. It has been argued that rehabilitation is more important for the final outcome than the initial treatment[64]. Even though the value of good rehabilitation is difficult to overestimate, there is still little knowledge in the literature of the best way of designing a rehabilitation protocol for both early and late rehabilitation[47, 77]. Brorsson recently published a thesis with the aim of improving rehabilitation[18]. The goal of rehabilitation is to optimise the conditions for tendon healing, as well as improving lower leg strength to help the patient return to pre-injury activities. Not surprisingly, it has been shown that early physiotherapy can improve both muscle function and patient-reported outcome[39]. Rehabilitation can be divided into four different phases[158]:

1. *The controlled mobilisation phase (0-8 weeks)*
2. *The early rehabilitation phase (6-11 weeks)*
3. *The late rehabilitation phase (10-15 weeks)*
4. *The return-to-sport phase (3-12 months)*

In the first phase, the foot is fixed either in a cast or in a brace. The aim during this phase is to create tendon apposition and stimulate the healing mechanism. In this early phase, weight-bearing and accelerated rehabilitation have been shown to be safe and to reduce the re-rupture rate and yield a better functional outcome[21, 146]. When the first phase is over, the brace is taken off and the patient enters the riskiest phase of rehabilitation. It is during the early rehabilitation phase that the risk of re-rupture is the greatest[120, 139]. Walking without a brace is started to stimulate healing, although the stretching of the tendon is avoided to prevent the elongation of the tendon[158]. The third phase focuses on building up strength in the lower leg muscles in order to prepare the tendon for more challenging motions. Heel rises and light running are started during this phase. Finally, return to sport is difficult to define, as many patients never return to their pre-injury activity. Usually, athletic patients are able to initiate running 16 weeks after the injury[108]. Before the patients can be recommended to return to sport, it is important to evaluate their muscle function and compare it with their healthy side, in a fashion similar to the way the functional testing has been done in this thesis. As with initial treatment, there is no consensus in terms of rehabilitation protocol and Frankewycz et al.[47] recently showed that there is a large variation in all phases of rehabilitation.

6.6 DURATION OF OPERATIVE TIME AND METABOLITES

Duration of operative time (DOT), i.e. knife time, can be highly variable and is associated with different outcomes. A longer DOT in bariatric surgery has, for example, been shown to be related to an increased complication rate, such as surgical site infections and deep venous thrombosis[3, 29, 32, 102, 168]. In hernia surgery, on the other hand, a longer DOT has been shown to correlate with a smaller risk of re-operation[175]. Whether the DOT can affect the metabolic healing response from surgical repair after tissue injury is unknown.

It is conceivable that a prolonged DOT may be associated with more surgical tissue trauma, resulting in an increase in cellular metabolism, which may enhance tissue repair, especially in hypovascular and sparsely metabolised musculoskeletal tissues, such as tendons. However, the DOT has not been compared with functional outcome in relation to tendon surgery. Repair after acute Achilles tendon ruptures is associated with the upregulation of essential metabolites such as, glycerol, glutamate, glucose, lactate and pyruvate, all involved in the healing process[56]. Specifically, glycerol, a marker of cellular damage[115], and glutamate, a metabolite/neurotransmitter, can promote wound healing[31, 122], but the correlation between the DOT on these metabolites is studied for the first time in this thesis.

Question

Does duration of operative time affect outcome? Is the length of the operative time associated with an upregulation of healing metabolites?

6.7 PREDICTORS OF OUTCOME

Previous research investigating outcome after an acute Achilles tendon rupture are inconclusive in terms of predictors[7, 14, 137, 159]. For instance, one study found poorer function and greater symptoms in women[159], while another[7] reported male gender, older age and deep venous thrombosis as predictors of poor outcome and a third found that a high body mass index (BMI) and older age were strong predictors of poorer patient-reported outcomes[137]. However, these previous studies are limited by small cohort sizes, implying the need for well-controlled studies comprising larger cohorts. This thesis aims to adress this and presents a predictor model including 391 randomised patients.

Question

Based on preoperative characteristics, is it possible to identify who will do well and who will do less well one year after an acute Achilles tendon rupture?

6.8. RESULTS AFTER AN ACUTE ACHILLES TENDON RUPTURE

6.8.1. RE-RUPTURE

A re-rupture is a serious complication, which has historically indicated the failure of treatment. Re-rupture has also been shown to be costly to society in terms of extended time off work and difficulty getting back to certain physically demanding professions[128]. However, little is known about the long-term outcome for patients with a re-rupture. The incidence has been shown to be approximately 12% in non-surgically treated patients and 0-5% in surgically treated patients[80]. However, in the study published by Olsson et al[138], there were no re-ruptures in the surgically-treated group and, in the RCT by Möller et al[120], only one. There are few previous studies that have evaluated the long-term outcome of Achilles tendon re-ruptures and these studies have included a small number of patients[119, 139, 142, 155]. In total, only 44 patients have been evaluated in all four studies, using non-validated outcome measurements and a heterogeneous study population, which makes it difficult to draw strong conclusions from the data.

All the studies show that patients have reduced strength in the injured tendon compared with the contralateral healthy tendon at follow-up. Moreover, a larger study comprising 28 patients, conducted by Nilsson Helander et al., also presented similar results[128]. This study included both re-ruptures and chronic ruptures[128]. Nilsson-Helander et al. used the same validated outcome measurements as those used in this thesis.

Question

What is the long-term consequence of a re-rupture?

6.8.2. ELONGATION

Regardless of the treatment and rehabilitation protocol, the ruptured tendon will have lasting weakness in the calf muscle and decreased force in active ankle plantar flexion[62, 63] which is still present 10 years after the injury[89, 117]. The reasons for these disappointing results are complex, but factors that are known to affect this are; calf muscle strength, ankle range of motion and the length of the tendon. There is also a relationship between these different factors. For instance, the elongation of the tendon leads to increased passive dorsiflexion and a decrease in active plantar flexion[33]. It is well known that the ruptured tendon elongates during healing, regardless of treatment, and this may explain some of the sustained weakness in active plantar flexion[163], figure VIII is a demonstration of an elongated tendon. It is possible that the best way to improve long-term outcome is to prevent this elongation by reducing tendon separation during early tendon loading and movement. Although surgery allows for the direct opposition of the ruptured parts of the tendon, this does not appear to prevent the elongation, as indicated by the minor differences in outcome between surgical and non-surgical treatment. This is a really challenging and interesting area of research where we still do not have an answer.

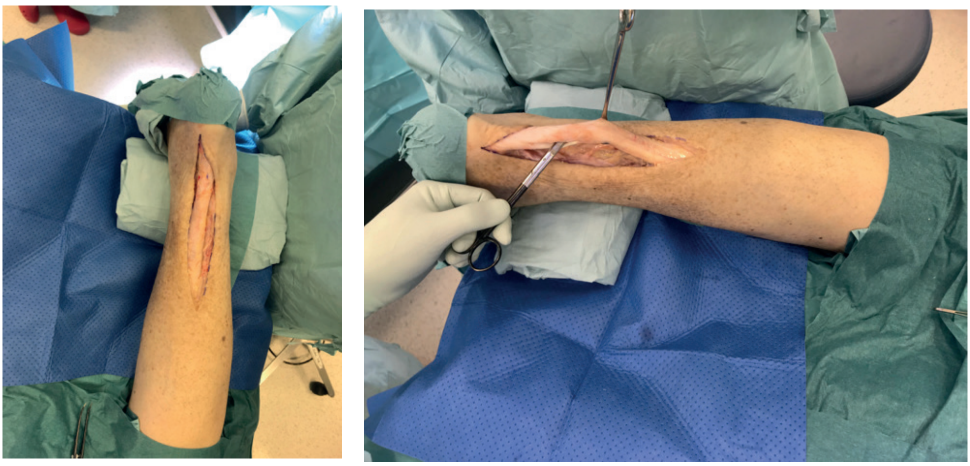


Figure VIII. *Intra-operative pictures of an elongated Achilles tendon*

6.8.3. HEALTH ECONOMICS

As medicine improves and we have more advanced treatment options, health costs continue to increase and this places more stress on health professionals to use the most cost-efficient treatments[132, 157]. In recent years, increased emphasis has been placed on physicians to consider the most cost-efficient treatment plans and, moreover, to consider the overall impact on society in terms of sick leave and quality of life. Costs are divided into direct and indirect costs. The direct costs are the cost of health care. These include all fixed costs, i.e. administration, staff salaries and accommodation at recovery, whereas the indirect costs are related to reduced work ability due to health reasons. A study by Ebinesan et al.[45] has evaluated the cost-efficiency of open Achilles tendon repair compared with non-surgical management. This study demonstrated that percutaneous and non-surgical management produced a significant cost reduction compared with open surgery. Another study by Carmont et al.[24] compared the open and percutaneous techniques. They found that the percutaneous technique resulted in lower direct costs with comparable clinical outcomes. However, the indirect cost was not investigated in this study. To the best of our knowledge, there are currently no work done comparing the cost of open repair and non-surgical management using early weight-bearing and a functional brace. As a result, there is a need for a study that includes all the costs associated with the management of these patients in order to evaluate the most cost-efficient treatment, especially as we know that there is little difference in clinical outcome between the groups. This thesis present the first cost-effectiveness analysis between surgical and non-surgical treatment.

Question

What is the total cost of treating an Achilles tendon rupture? Which treatment is the most cost-effective?

6.8.4. MAPPING

Cost-effectiveness analyses are being used increasingly to inform decision makers with regard to setting priorities in health care. Comparing and ranking treatments based on the cost per gained QALY (the lower, the better) could indicate how to maximise patient health benefits given limited health-care budgets[80]. The QALY is a health outcome metric that combines health-related quality of life (HRQoL) and "quantity" of life (life length). One QALY can be viewed as one year lived in the best possible health state. The HRQoL used to calculate QALYs is (typically) based on patients' self-assessed valuations of different health states and is often referred to as a preference-based measurement[152]. Different types of preference-based instrument are used to measure the preference-based HRQoL score. These instruments can be condition specific, but they are commonly generic, i.e. suitable in theory for all kinds of health-care treatment, and include the EQ-5D, the six-dimensional health state short form[16] and the Health Utilities Index[65]. There is no consensus on which preference-based measurement should be used in cost-effectiveness analyses, although the EQ-5D has become increasingly recognised[16]. The problem that another score has been used has been encountered multiple times in clinical studies[16], where a non-preference-based measurement has been the only suitable health measurement available for the condition in question. To solve this problem, a method known as mapping is being used more frequently[37, 101, 104]. Mapping investigates the statistical relationship between a non-preference-based measurement and a preference-based measurement, producing an algorithm ("map") to be used in the calculation of a preference-based HRQoL score. To make this feasible, the method requires a data set of the source measurement (e.g. the ATRS) and the target measurement (e.g. the EQ-5D) that have been administered alongside each other to the same patients in the relevant clinical trial[16, 178]. If a statistical association between the ATRS and the EQ-5D can be established, i.e. allowing the ATRS to be directly applicable for cost/QALY analyses, it will be valuable in the assessment of treatment for total Achilles tendon rupture.

Question

Is it possible to use mapping to convert the ATRS to the EQ5D?

7

AIMS

This thesis aims to determine important predictors of outcome in patients with Achilles tendon ruptures in order to be able to help patients and surgeons to make the best possible choice between surgical and non-surgical management. It also aims to investigate the relationship between cellular metabolism and tendon healing, the long-term effect on function and symptoms and the ability to be physically active after an Achilles tendon re-rupture. Finally, the aim is to perform a cost-efficiency analysis between surgical and non-surgical management.

7.1 OBJECTIVES

Study I: The aim of this study is to investigate whether acute US can be used to predict the risk of re-ruptures and outcomes after treating an acute Achilles tendon rupture.

Study II: The aim of this study is to evaluate the influence of duration of operative time on specific healing metabolites, as well as functional outcome in patients treated surgically for an acute Achilles tendon rupture.

Study III: The aim of this study is to determine the long-term functional and subjective outcome following a re-rupture of the Achilles tendon.

Study IV: The aim of this study is to determine the actual cost of an acute Achilles tendon rupture and compare the direct and indirect costs of surgical and non-surgical management of an Achilles tendon rupture.

Study V: The aim of this study is to develop an algorithm to convert the Achilles tendon total rupture score (ATRS) to the EuroQol-5D score.

Study VI: The aim of this study is to determine the predictors of functional and patient-reported outcome one year after an acute Achilles tendon rupture.

8

METHODS

8.1 MUSCLE FUNCTION

FUNCTIONAL TESTS

Single-leg standing heel rise

A standing single-leg heel rise has been widely used as a tool for the functional evaluation of calf muscle endurance after an Achilles tendon rupture[161], see figue IX. It has been proven to be both valid and reliable[22, 160]. The test is performed with the patient standing on one foot on a 20 cm flat box with a 10-degree incline, always starting with the healthy side first. The patient is then instructed to raise his/her heel as high as possible and a metronome is used to keep the tempo at 30 heel rises a minute. A linear encoder unit connected to the MuscleLab® (Ergotest Technology, Oslo, Norway) system is used. The linear encoder has a string which is attached to the patient's shoe and measures both the height and the number of heel rises. This system is also able to calculate the heel rise work after adjusting for the patient's weight. The test is ended when the patient is unable to perform more heel rises. The critical number for good function is regarded as 25 repetitions; however, there is large variability[103].

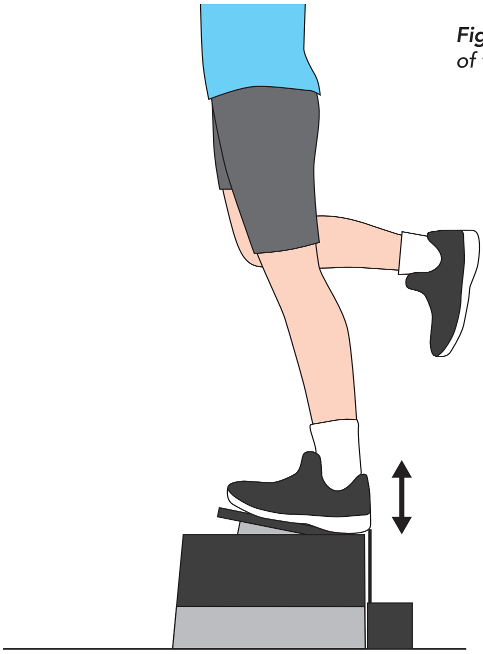


Figure IX. *Illustration of the heel-rise test*

Jump tests

Jump tests play a central role in Achilles tendon functional evaluation. The most important tests are hopping and the drop counter-movement jump (Drop CMJ), which have previously been validated and shown to have excellent reliability[127, 138, 160]. Like the heel-rise test, the healthy side is tested first. Hopping is performed by asking the subject to stand on one leg with his/her arms at his/her side and perform a skipping-like jump at a self-selected speed, figure X. Twenty-five jumps are performed and recorded. The middle 20 jumps are used to calculate the mean hopping height and the plyometric quotient (mean flight time/contact time). The drop CMJ is a more demanding test. It is performed by the subject standing on a 20 cm flat box on one leg with his/her hands behind the back. A jump is then made from the box to the floor and, as soon as he/she hits the floor, he/she is instructed to perform a maximum vertical jump, figure X. At least three jumps are performed and the highest is used for analysis. For both tests, a light mat connected to the MuscleLab® (Ergotest Technology, Oslo, Norway) system is used.

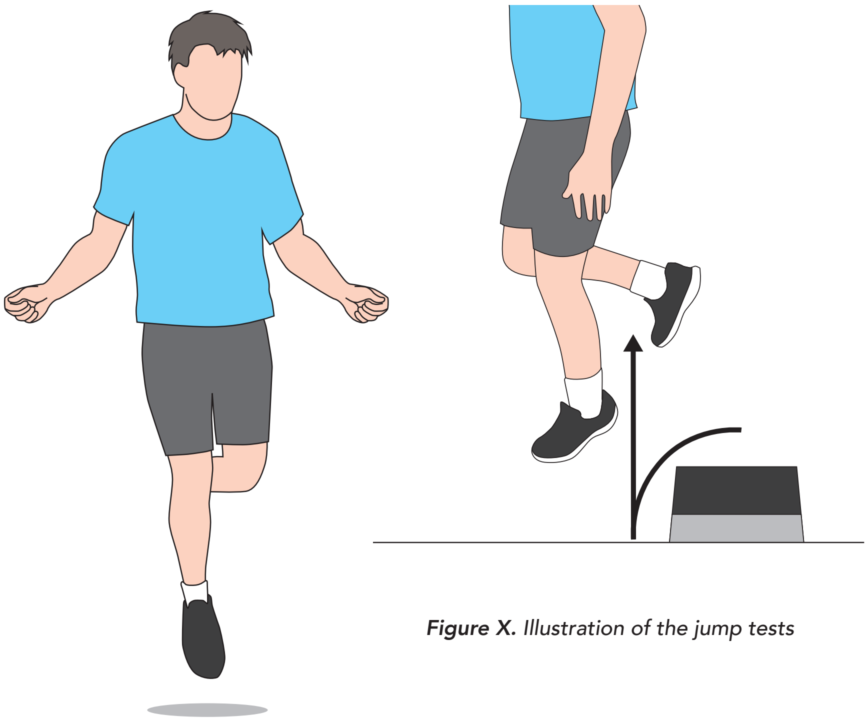


Figure X. *Illustration of the jump tests*

Strength and power tests

Strength and power tests for concentric and eccentric force are performed by the patient standing in a weight training machine and performing a single-leg heel rise. Patients are told to raise their heel as quickly and forcefully as possible and the knee is not allowed to flex more than 20 degrees, the test is illustrated in figure XI. This is then repeated three times with the patient's body weight plus 13 kg for the first test. Another 10 kg are then added and the test is stopped when a decrease in the patient's power output is noted. The max power in watts is recorded as the result. Just like heel-rise height, a linear encoder is attached to the patient's shoe and standardised equipment is used. The linear encoder unit is connected to MuscleLab® (Ergotest Technology, Oslo, Norway). This test has been shown to be reliable and valid[160]. Table I illustrates which functional tests are used in the different studies.

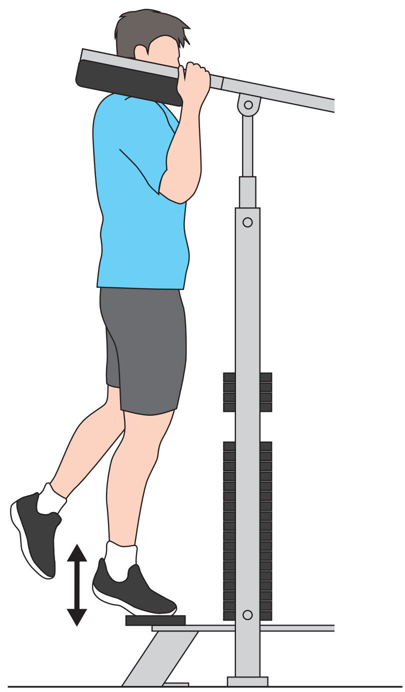


Figure XI. *Illustration of the power test*

Table I. Different functional tests used in the studies presented in this thesis

Test	*Study I*	*Study II*	*Study III*	*Study IV*	*Study V*	*Study VI*
Hopping	√		√			
Drop CMJ	√		√			
Concentric power			√			√
Eccentric power			√			
Heel-rise repetitions	√	√	√			√
Heel-rise height		√	√			√
Heel-rise work	√	√	√			√

8.2 PATIENT-REPORTED OUTCOME MEASUREMENTS (PROMS)

Achilles tendon total rupture score (ATRS)

The ATRS is an injury-specific outcome score for patients treated for Achilles tendon ruptures. A Likert scale is used. Patients' answers are scored from 0-10, where one means significant symptoms and difficulty with physical activity and 10 indicates no symptoms or difficulty with physical activity. One hundred is the maximum score and indicates a patient without any symptoms/difficulty with physical activity. The ATRS has been shown to have good reliability and validity[129]. The ATRS has been translated to and validated for several different languages including English[26]. See the appendix.

The foot and ankle outcome score (FAOS)

The FAOS is a validated score that was developed to assess the subjective outcome for patients with foot and ankle problems[148]. It has not been used for Achilles tendon ruptures, but it has been widely used for patients with ankle instability, Achilles tendinopathy and plantar fasciitis. It is based on the knee injury and osteoarthritis outcome score (KOOS) and was validated on 213 patients with ankle instability[148]. The FAOS has five subscales: pain, other symptoms, function in daily living (ADL), function in sport and recreation (Sport Rec) and foot- and ankle-related Quality of Life (QOL). Answers are given as 0-4 for each subgroup with 4 representing no problems and 0 severe limitations. See the appendix.

Physical activity scale (PAS)

This is a six-level questionnaire that was initially published in 1988[58]. The score has been widely utilised for research purposes for a long time[59]. In this thesis, a modified six-level questionnaire has been used, which was initially designed to measure activity in the geriatric population. Level one indicates very limited activity, while level six indicates several hard workouts a week. See the appendix.

EuroQol-5D (EQ-5D)

The EQ-5D is a generic instrument for measuring overall health-related quality of life based on five dimensions (mobility, self-care, usual activities, pain/discomfort and depression/anxiety) and includes three levels (none, moderate and severe problems) of answers and a rating scale[179]. The EQ-5D is scored on an index scale of 0 to 1.0 (English version), where 1.0 corresponds to a totally healthy person and 0 is equal to death. A difference of 0.03 or more is regarded as clinically relevant. It was intended to be used for economic analysis (cost-utility analysis) and to be able to calculate the cost per quality-adjusted life year (QALY). Brazier et al.[15] evaluated the EQ-5D in a group of patients with osteoarthritis of the knee and concluded that it could be used for economic evaluations after surgery. See the appendix.

Table II. Different patient-reported outcomes used in the studies presented in this thesis

PROM	*Study I*	*Study II*	*Study III*	*Study IV*	*Study V*	*Study VI*
ATRS	√	√	√		√	√
FAOS		√	√			
PAS		√	√			
EQ-5D				√	√	

8.3. CLINICAL MEASUREMENTS

Achilles tendon resting angle (ATRA)

The ATRA was described and validated by Carmont et al.[25]. It is performed with the patient in a prone position, with the knee flexed at 90 degrees. The patient is instructed to relax his/her leg. A goniometer (Medi GmbH, Bayreuth, Germany) is placed with one arm along the shaft of the fibula, directed towards the centre of the fibular head. The other arm is centred on the head of the fifth metatarsal. The angle between the arms is measured. This measurement has been shown to have excellent reliability (ICC 0.92 (CI [0.83–0.97]). Moreover, it has also been found to correlate with the ATRS and heel-rise height in patients with an Achilles tendon rupture[25].

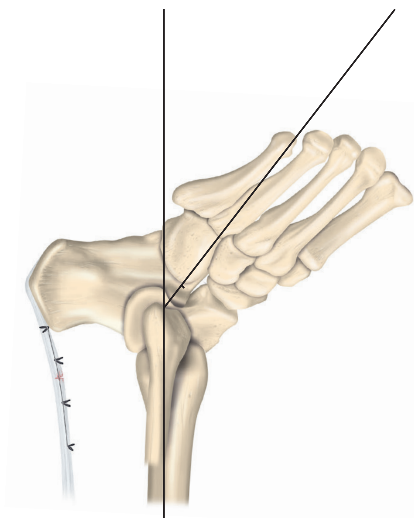


Figure XII. *Illustration of Achilles tendon resting angle (ATRA)*

Dorsiflexion range of motion and calf circumference

The patients' ability to dorsiflex their ankle joint was measured using an goniometer, with the technique described by Munteanu et al.[124]. The subject stands, positioning the leg to be tested behind as far as possible without lifting the heel, and is then asked to lean forward until maximum stretch is felt in the calf muscle. The test is performed with the knee both straight and flexed.

The calf circumference was measured at the largest area of the calf muscle with a standard tape measured with one mm increments. The patient is positioned in a prone position with the knee straight. Care is taken not to compress the calf while performing the measurements. Repeated measurements are made until the same value is found for successive measurements[25].

8.4. SURGICAL TECHNIQUES IN THIS THESIS

Primary ruptures (I)

The surgical technique used in Studies I and II and for some of the patients in Study VI was as follows. The surgery was performed with the patient in a prone position under local, spinal, or general anaesthesia. A tourniquet was used for haemostasis in approximately 25% of patients. After a longitudinal 5- to 8-cm medial skin and paratenon incision, an end-to-end suture was placed using a modified Kessler suture technique and 1-0 polydioxanone (PDS) sutures (PDS II, Ethicon, Somerville, New Jersey). The paratenon was carefully repaired and the skin closed with interrupted nylon sutures[127]. Postoperatively, the patients were placed in a below-the-knee cast with the foot in an approximately 30-degree equinus position.

Primary ruptures (II)

The surgical technique used in Studies IV and VI was described by Olsson et al.[138] as a standardised technique. All the procedures were performed under local anaesthesia and prophylactic antibiotics (cloxacillin) were administered. Because of the high risk of deep venous thrombosis (DVT), prophylactic dalteparin was administered to all patients. Patients were operated on in a prone position, without a tourniquet. Through a postero-medial incision, the paratenon was divided. The rupture site was identified and repaired using end-to-end core sutures with two strong, semi-absorbable sutures (No. 2 Orthocord, DePuy Mitek, Norwood, Massachusetts, USA), using a modified Kessler technique. A running circumferential suture with absorbable sutures (No. 0 Polysorb, Tyco, Norwalk, Connecticut, USA) was used, with an epitendinous cross-stitch technique described by Silfverskiold and Andersson to reinforce the core sutures[164]. The paratenon was closed with absorbable sutures. The skin was closed with interrupted nylon sutures. Postoperatively, the ankle was placed in a pneumatic walker brace (Aircast XP Diabetic Walker, DJO Global, Carlsbad, California, USA) including three heel pads to create an angle of 22 degrees. Patients were allowed full weight-bearing in this functional brace from the first postoperative day. All patients were treated with a brace for six weeks.

Re-ruptures

The following surgical technique was used in Study III[182]. This surgical technique was described by Nilsson-Helander et al.[128]. All patients were operated on under spinal or general anaesthesia and antibiotics were administered preoperatively. With the patient in a prone position, a central approximately 20 cm long incision, curved slightly medially and distally to protect the sural nerve, was made. A modified Kessler suture was used to adapt the tendon ends after debridement. A free flap from the gastrocnemius aponeurosis was used and the size was dependent on the tendon gap. The free flap covered the end-to-end suture, secured with 3-0 PDS sutures. Postoperatively, a below-the-knee cast was used with the foot in the equinus position. After six weeks, an adjustable brace (Don-Joy ROM-Walker) was used for a further two weeks, with range of motion from neutral to free plantarflexion. Weight-bearing was allowed after six weeks. An experienced physiotherapist was responsible for the rehabilitation. figure XIII is an illustration of the surgical technique.

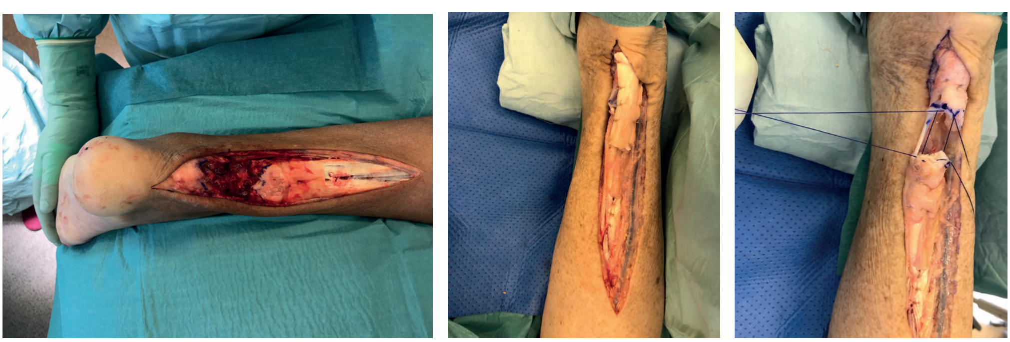


Figure XIII. *Intra-operative pictures of a repair of an Achilles tendon re-rupture. A free gastrocnemius flap is used*

8.5. ULTRASONOGRAPHY

TENDON LENGTH

In Study III, the LOGIO e Ultrasonography (US) (GE Healthcare) system with a wide-band linear array probe (5.0-13.0 MHz) was used to measure tendon length. All the images were recorded using the EFOV feature and 10 MHz B-mode. A picture demonstrating the osteotendinous junction at the calcaneus and the musculotendinous junction of the gastrocnemius was obtained. Three images that fulfil the above criteria were saved and measurements were made using the same US machine. The participants were asked to lie down in a prone position with their hips and knees straight and their ankles hanging over the end of the examination table. The examiner placed light tension on the Achilles tendon by stabilising the foot and used the other hand to move the transducer slowly from the heel in a straight line along the tendon and mid-portion of the calf. This measurement method has been shown to have excellent reliability, with an ICC of 0.987-0.997 and a MDC of 0.43[162]. The length has been correlated with heel-rise height up to one year after an Achilles tendon rupture[162]. Figure XIV illustrates how the measurement is done.

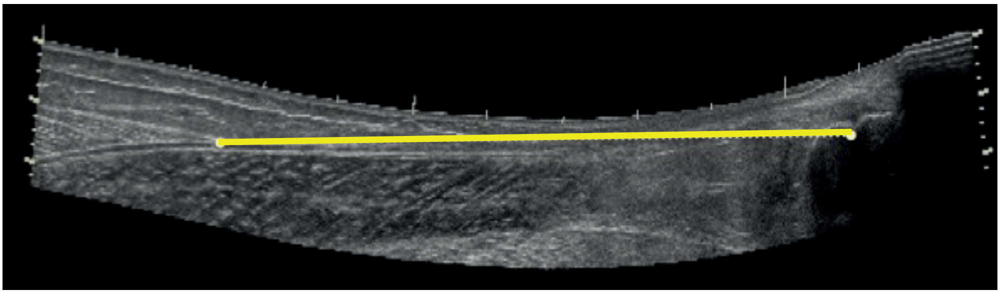


Figure XIV. Picture of how to measure the length of the Achilles tendon

ULTRASONOGRAPHY ASSESSMENT OF TENDON GAP

This method was used in Study I and was performed by one of two experienced radiologists using a Siemens Sonoline Antares (Siemens Healthcare Global) equipped with a Variable Frequency (VF) 13.5 mHz multifrequency linear array transducer, using a 11.4 mHz default setting and scanning parameters designed for superficial musculoskeletal scanning. Scanning of the Achilles tendon was performed in both the longitudinal and axial planes assisted by dynamic scanning during passive ankle motion to facilitate the identification of rupture. Moreover, extended field-of-view scanning (SieClear, compound scanning) was performed to illustrate the tendon gap and all measurements were performed using real-time scanning. No stand-off pads were used and scanning was performed with the ankle in both neutral and approximately 30 degrees of passive plantar flexion. Frank anechoic tendon defects or tendon discontinuities of the fibrillary echo texture were direct criteria of tendon tears. The gap between the two tendon ends was measured in approximately 30 degrees of plantar flexion at the centre of the tendon gap and graded as 0-5mm, 5-10 mm and >10mm. These groups were used to evaluate whether there was a difference in re-rupture occurrence between the groups. Figure XV is an illustration of this.

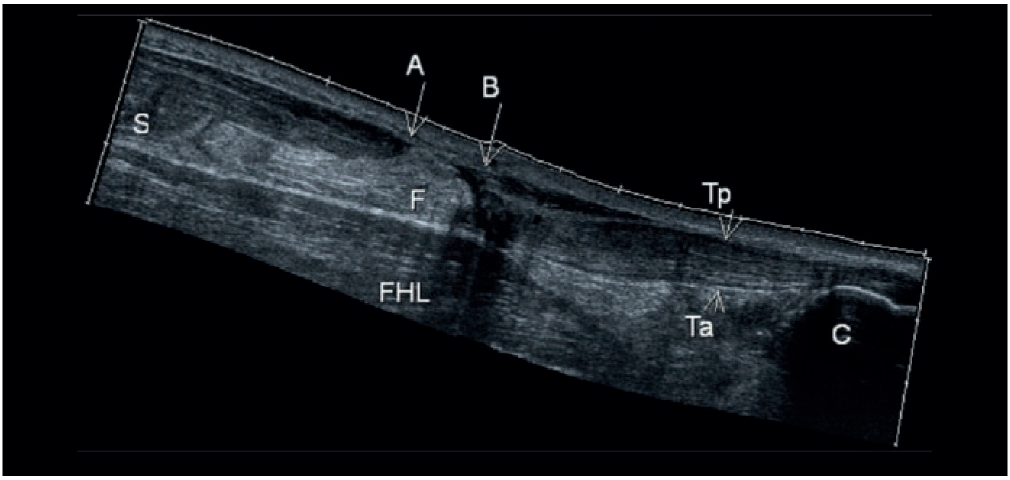


Figure XV. *Picture of a gap in a ruptured tendon.*
C, calcaneus; F, fat tissue; FHL, flexor hallucis longus muscle; S, soleus muscle; Ta, anterior tendon surface; Tp, posterior tendon surface. Figure is from Orthopedic Journal of Sports Medicine, 2016 Oct 4(10), 2325967116667920

8.6. MICRODIALYSIS

Microdialysis was used to measure the healing metabolites (glycerol, glutamate, glucose, lactate and pyruvate). This measurement was performed in Study II and was made by placing the patient in a prone position, while the skin covering both Achilles tendons was sterilised. The calcaneus was identified and the microdialysis catheter (CMA 71; CMA Microdialysis AB, Solna, Sweden; (100 kDa molecular cut-off membrane, 0.5 mm outer diameter; 30 mm in length) was inserted 1.5-3 cm proximal to the calcaneus and 1 cm lateral to the Achilles tendon. Using ultrasound guidance, the catheter membrane was inserted as close to the site of rupture as possible in the paratendinous space and thereafter at the same level on the contralateral side. After insertion, Macrodex® perfusion fluid was induced via the tip of the catheter and the semi-permeable catheter membrane into a vial. Four vials were collected from each tendon, with a flow rate of 1.0 µL/min and two vials/hour, and analysed within five days using an ISCUS Clinical Microdialysis Analyzer. The first vial was consistently discarded, as the insertion of the catheter might alter the concentrations of the substances in the tendon. The other vials were used to calculate individual and overall mean concentrations of individual substances or ratios, which were used for statistical analysis.

8.7. HEALTH ECONOMICS

Quality-adjusted life years

A quality-adjusted life year is a measurement that combines health-related quality of life and life expectancy in one metric[17]. Quality of life is measured on an index that is anchored so that 1 represents the best possible health state and 0 represents "equal to being dead", while life expectancy is measured in years. In terms of interpretation, one QALY is equivalent to living one year in the best possible health state. In health-economic evaluation methods (cost-effectiveness/utility analyses), the QALY is the most commonly used outcome metric. It was intended to be used for economic analysis, where the cost per QALY could be assessed and compared across treatments. Life expectancy is not affected by the surgical or non-surgical treatments, hence any difference in the number of gained QALYs is due to differences in health-related quality of life, "QALY weight". The "QALY weight" was assessed using the EuroQol-5 Dimension Questionnaire instrument, which is a generic instrument using which patients self-report their health status based on five dimensions (mobility, self-care, usual activities, pain/discomfort and depression/

anxiety), including answers on three levels (none, moderate and severe problems). The EQ-5D answers were scored on the index scale based on the UK tariff, with a range of -0.59 to 1 (Dolan algorithm). Brazier et al.[15] evaluated the EQ-5D in a group of patients with osteoarthritis of the knee and concluded that it could be used for economic evaluations of surgery. The discrepancy in QALY can be illustrated by figure XVI, which represents the difference in the area under the curve between the black and grey line. Quality-adjusted life year calculations were made at patient level, reflecting the change from baseline to three, six and 12 months.

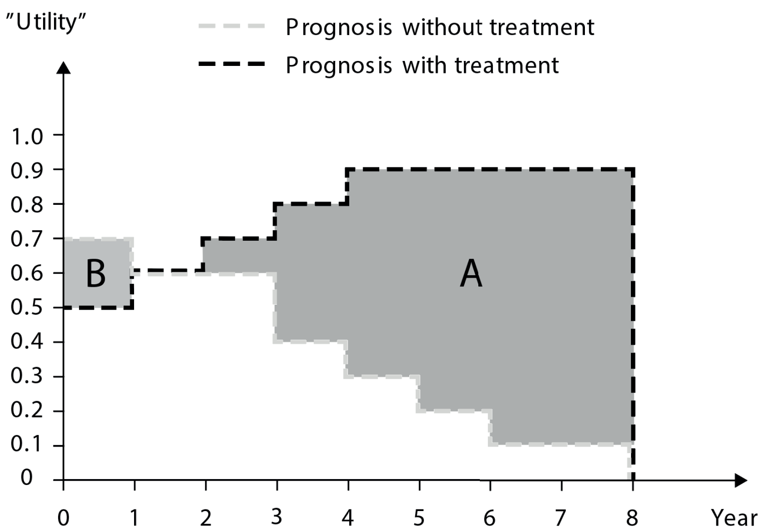


Figure XVI. *Diagram of QALY calculation between two alternative treatments*

Economic costs

The economic costs were categorised as either direct health-care costs or indirect (productivity) costs. The direct costs include resource use for administration, staff salaries and accommodation at recovery. Moreover, they include patient-specific expenses such as examination, surgery (operating room (OR) including anaesthesia and material), postoperative visits, rehabilitation, laboratory tests, and imaging. All the costs were collected from the hospitals' accounting databases. See Table III for the list of resource use items and the associated unit costs. Productivity loss was based on the number of sick-leave days. The human capital method was used to assess the value of production loss due to sick leave, which implies that each hour of production loss is valued by the gross wage, including social fees (i.e. the market price in the sense that this is what the employer pays per hour). Data on the number of sick-leave days were self-reported at the follow-up. The costs are presented in euros using 2013 exchange rates for conversion from Swedish kronor (8.86 SEK = 1 euro).

Table III. Resource use units and cost per unit

Item	***Cost (euros)***
Visit to ER	209
Physiotherapy visit	62
Inpatient night	536
Day surgical bed	267
Surgeon cost per minute	5.6
Operation cost per minute	16.2
Outpatient clinic visit	185
MRI scan	399
Ultrasound scan	267
Prescription drugs	75

Cost-effectiveness analysis

The cost-effectiveness of the surgical treatment was compared with that of the non-surgical treatment based on the incremental cost-effectiveness ratio (ICER) from a societal perspective (including productivity effects)[34]. The ICER is calculated as:

$$\frac{\text{Cost}_{\text{surgical}} - \text{Cost}_{\text{non-surgical}}}{\text{QALY}_{\text{surgical}} - \text{QALY}_{\text{non-surgical}}} = \text{ICER}$$

The ICER can be interpreted as the cost of obtaining one extra QALY and enables comparisons between interventions in all areas of health care. We did not discount health benefits or costs in this thesis, as we used a 12-month time horizon.

To demonstrate the sampling uncertainty that surrounds the mean ICER, a non-parametric bootstrapping (with replacement) was conducted. Bootstrapping is when a smaller population is resampled into a larger one by randomly drawing samples.

9

SUBJECTS

Table IV. Table of randomised controlled trials for subjects presented in this thesis

	Study I	***Study II***	***Study III***	***Study IV***	***Study V***	***Study VI***
Nilsson-Helander et al.	n=45	n=49	n=2			n=97
Olsson et al.				n=100	n=100	n=100
Domeji-Arverud et al.		n=150				n=150
Domeji-Arverud et al.						n=40
Svedman et al.						n=95
Valkering et al		n=58				

9.1. STUDY I

The participants in this study came from the RCT published by Nilsson-Helander et al. in 2010. Unfortunately, only 45 of the 97 could be included, due to hospital re-organisation during the study period. The average age was 37 years, range (23-59), and 37 males and eight females were included. The inclusion criteria were any patients with a complete unilateral midsubstance acute Achilles tendon rupture with treatment initiated within 72 hours from injury. The exclusion criteria were diabetes mellitus, previous Achilles tendon rupture, other lower leg injuries, immunosuppressive therapy and neurovascular disease. None of the included patients had a medical history of either fluoroquinolone use or corticosteroid injections in the area.

9.2. STUDY II

Two hundred and eight patients were included from two different randomised controlled trials at Karolinska University Hospital, Stockholm, Sweden. Patients who had sustained an acute unilateral rupture of the Achilles tendon were eligible for inclusion. The exclusion criteria were: current anticoagulation treatment (including high-dose acetylsalicylic acid), known kidney failure, heart failure with pitting oedema, thrombophlebitis, thromboembolic event during the previous three months, known malignancy, haemophilia, pregnancy, other surgery during the previous month, inability to follow instructions or planned follow-up at another hospital. All the patients were operated at the Karolinska University Hospital, Stockholm, by the surgeon responsible for outpatient surgeries that day. Accordingly, the patients were not able to request a specific surgeon. Patients were enrolled and assigned to the postoperative interventions by a research nurse or a third-party nurse. Randomisation to postoperative treatment was performed using computer-generated random numbers in permuted blocks of four, through an independent software specialist, and consecutively numbered, sealed, opaque envelopes were opened after surgery and prior to treatment. At two weeks post-operatively, microdialysis was performed on the Achilles tendon of both limbs in 70 patients who consented to undergo microdialysis. At a three-month follow up, 130 patients filled out the Achilles tendon total rupture score. Additionally, at the 12-month follow up, 156 patients filled out the ATRS, foot and ankle outcome score and physical activity scale criteria.

To confirm the data from the internal cohort of 208 patients, ATRS data at six months postoperatively from an external cohort of 49 ATR patients from Sahlgrenska University Hospital in Gothenburg, Sweden, were included in the analyses. These patients were part of a randomised controlled trial comparing surgical and non-surgical treatment with early mobilisation, using a modified Kessler suture technique. Anaesthetic methods varied between local, spinal and general anaesthesia.

9.3. STUDY III

The patients for this study were collected from both Sahlgrenska University Hospital and Kungsbacka Hospital. Notes were reviewed to identify all re-ruptures over a 10-year period. Fifty-two patients were identified and 24 of them agreed to participate. Four patients were excluded because they did not fit the study inclusion criterion. One had bilateral ruptures, two had chronic ruptures and one had a recent ankle fracture, which made the evaluation impossible. A total of 20 patients (16 males) with a mean (SD) age of 44 (10.9) years were included in the study. The inclusion criterion was any patients with a unilateral Achilles tendon re-rupture within the last 10 years. The exclusion criteria were age more than 70, diabetes mellitus, other injuries affecting the limb, neuromuscular disease, peripheral vascular disease, immunosuppressive therapy and inability to perform the follow-up evaluation. The initial treatment of the re-rupture group was mixed, with non-surgical (n = 18), with a cast for two weeks, followed by early weight-bearing in a walker brace for six weeks, and surgical (n = 2), with a below-the-knee cast for two weeks, followed by a walker brace for another six weeks. The mean follow-up from the time of the index injury for re-ruptures was 50.9 (38.1) months.

9.4. STUDY IV

One hundred patients were included and their median age was 40 years, range (18-65 years), 86 males and 14 females. Randomisation was performed directly after inclusion and computer-generated opaque, sealed envelopes were used. One of the surgical patients was excluded due to a partial re-rupture and five surgical patients were lost to the one-year follow-up. One patient was excluded due to incorrect inclusion and one was lost to the one-year follow-up in the non-surgical group. All patients (age, 18-65 years) with a closed midsubstance rupture, who attended this centre, were included in the study. The diagnosis was based on medical history and clinical examination (a palpable gap and a positive Thompson test). Patients were excluded if the rupture was older than four days and if they had a prior Achilles tendon rupture (either side) or other injuries that affected their lower limb function. Neuromuscular disease, diabetes mellitus, peripheral vascular disease, immunosuppressive treatment including systemic cortisone, skin infection or wound and inability to attend rehabilitation or evaluations were all exclusion criteria.

9.5. STUDY V

The patients in Study V are the same as in Study IV.

9.6. STUDY VI

From the 482 patients eligible from the different cohorts, 391 patients (83%) were included in the analysis, while 89 patients (17%) were excluded due to missing follow-up data. The mean age of the included cohort was 40.4 (range 18-71) years and 17% were women. Seventy-nine percent of the cohort were treated with surgery.

10

ETHICAL APPROVAL

Ethical approval for all studies was applied for and approved by the regional ethical boards in Gothenburg and Stockholm, Sweden.

11

STATISTICAL METHODS

11.1. STUDY I

The limb symmetry index (LSI) was calculated to compare the two treatment groups. The LSI was defined as the ratio between the involved limb score and the uninvolved limb score, expressed as a percentage: LSI (result of involved/result of uninvolved x 100 = LSI). The three groups (0-5 mm, >5-10 mm and >10 mm) were used to compare the occurrence of re-ruptures. When comparing re-ruptures, a Pearson's chi-square analysis of the three groups was performed. A positive predictive value was calculated as the patients in the group with a re-rupture divided by all the patients in the group. At the 12-month follow-up, the >10 mm group only consisted of two patients, as three of the five had suffered a re-rupture and were therefore not included in the 12-month follow-up. It was therefore decided to merge the remaining two patients from the >10-mm group into two groups (5 mm, >5 mm) for the 12-month follow up. The Mann-Whitney U-test was performed to compare the two groups at the 12-month follow-up. Moreover, one patient was unable to attend the 12-month follow-up due to systemic illness and was therefore excluded.

11.2. STUDY II

The variables were summarised with standard descriptive statistics such as the mean, standard deviation (SD) and frequency. All the variables were checked for skewness. Comparisons between groups were performed using ANOVA for repeated measurements and an independent Student's t-test when appropriate. Correlations between different variables and outcome were expressed as Pearson's correlation coefficients. A non-parametric Spearman's rank correlation was used if a distribution was severely skewed. For outcome variables that were normally distributed and significantly correlated with duration of operative time, multiple linear regression analyses (stepwise forward method, with an inclusion level of 0.05) were conducted. This was done in order to investigate the unique relationships between the independent variables (gender, age, height, weight, BMI, surgeon experience, the time from injury until operation, DOT and postoperative treatment) and the dependent variable.

11.3. STUDY III

The limb symmetry index was defined as the ratio between the involved limb score and the uninvolved limb score, expressed as a percentage. The LSI was calculated and compared with the two-year results from the primary Achilles tendon rupture group. A non-parametric test was used, as the data were not normally distributed. The healthy side was compared with the injured side using Wilcoxon's signed rank test. Effect size was calculated using Cohen's d. To compare the re-ruptures with primary ruptures, the Mantel-Haenszel chi-square exact test was used for ordered categorical variables, while the Mann-Whitney U-test was used for continuous variables.

11.4. STUDY IV

Summary statistics are given in terms of means and standard deviations (continuous variables) and proportions (dichotomous variables). Tests of differences in means were conducted by t-tests (continuous variables) and equality of proportions using large-sample statistics. It is well known that health-care cost data are typically not normally distributed (right-skewed) and we therefore performed sensitivity tests based on logarithmic transformations.

11.5. STUDY V

The best statistical algorithm to map scores from the ATRS to EQ-5D utility scores was based on the K-Fold cross validation approach with 10 folds (K=10). This implies that the data set is split into 10 sub-samples and the different algorithms tested were developed based on regression analyses on nine of the sub-samples (training samples) and subsequently tested on the remaining (10th) sub-sample (validation sample). This approach is iterated so that each of the 10 sub-samples acts as the validation sample once. Each algorithm was evaluated based on the absolute difference between the predicted and actual outcomes in the validation sample and the algorithm with the smallest error in prediction is chosen as the best performing algorithm.

11.6. STUDY VI

Continuous variables were described with the mean, standard deviation (SD), median and range and categorical variables with count (n) and proportions (%). The results of the tests of muscle function were reported as a limb symmetry index, defined as the ratio between the involved limb score and the uninvolved limb, expressed as a percentage (result of involved/result of uninvolved x 100 = LSI). For comparisons between included and excluded patients, Fisher's exact test (lowest one-sided p-value multiplied by 2) for dichotomous variables and the Mann-Whitney U-test for continuous variables were performed. Distributions of outcomes were checked with box plots. In cases of non-linear distribution, Spearman's rho was used to determine correlations between predictor and outcome. In addition, outcomes were compared with the Mann-Whitney U-test stratified by the dichotomous predictor. Linear regression modelling was performed to analyse the effect of patient demographics on the LSI of the different tests of muscle function.

The results of the linear regression were reported with beta estimates, 95% confidence intervals (CI) and p-values. The R-square was given as a measurement of the goodness of the model. The likelihood of reporting in the top or bottom ten percentiles of the ATRS and LSI in heel-rise height was analysed with binary regression modelling. Patient demographics and treatment were used as independent variables. The results of the binary regression models were presented with odds ratios (OR), 95% CI and p-values. An OR is expressed for every unit increase in the predictor variable. All significance tests were two-sided and conducted at the 5% significance level. Forward stepwise multivariate regression modelling was planned in cases where more than one predictor was found to be significant.

12

RESULTS AND SUMMARY OF THE STUDIES

12.1 STUDY I

Acute ultrasonography investigation to predict re-ruptures and outcomes in patients with an Achilles tendon rupture

INTRODUCTION

The optimal treatment for acute Achilles tendon ruptures is still the subject of an ongoing debate. Acute ultrasonography investigations to measure the diastasis between the tendon ends have previously been used to classify acute Achilles tendon ruptures; however, no study has used US to predict the risk of re-ruptures, as well as functional and patient-reported outcome.

PURPOSE

To investigate whether acute US can be used to predict the risk of re-ruptures and outcomes after treating an acute Achilles tendon rupture.

METHODS

Forty-five patients (37 men, eight women) with a mean age of 39 ± 9.2 years (range 23-59 years) from a cohort of 97 patients participating in a randomised controlled study comparing surgical and non-surgical treatment were included. Ultrasound was performed within 72 hours from the index injury. The diastasis between the tendon ends was documented. Re-rupture was the primary end-point and the patients' functional and patient-reported outcomes were measured at 12 months post-injury. A flow chart of the study is shown in figure XVII.

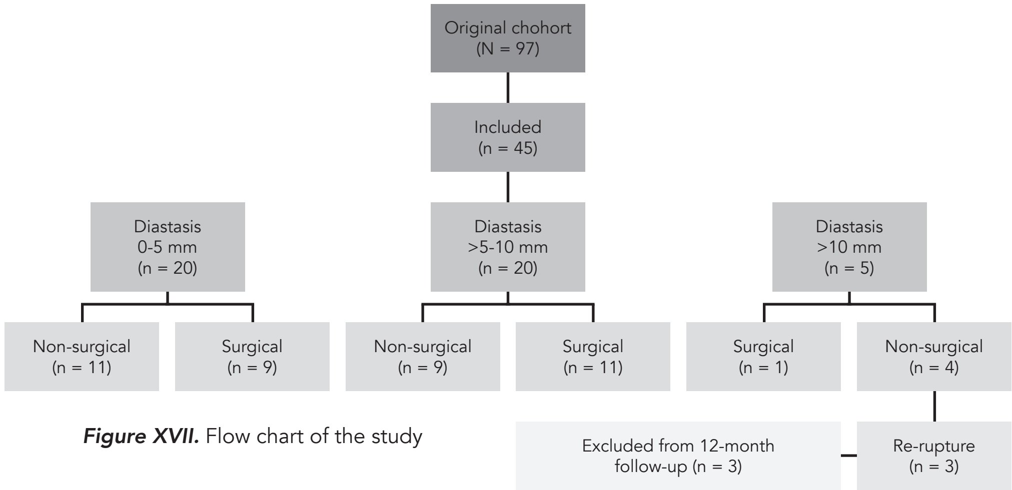


Figure XVII. Flow chart of the study

RESULTS

Table V demonstrates number of patients in each diastasis group. Patients with a diastasis of > 10 mm who were treated non-surgically had a higher degree of re-rupture. In the non-surgically-treated group, three of four (75%) patients with a diastasis of > 10 mm suffered a re-rupture ($p<0.001$). Moreover, in the non-surgical group, there was a significantly poorer outcome in patients with a diastasis of > 5 mm in terms of patient-reported outcomes using the ATRS ($p = 0.004$) and heel-rise height at 12 months ($p=0.048$) compared with the group with a lesser degree of tendon separation. Table VI demonstrates the difference in outcome with the patients stratified by treatment and diastasis of more than 5 mm.

Table V. *Patients divided into diastasis groups*

Treatment	*≤5mm diastasis*	*>5 -10mm diastasis*	*>10mm diastasis*
Non-surgical (n)	11	9	4
Surgical (n)	9	11	1
Total	20	20	5

Table VI. *Results for patients with a diastasis of >5mm with different treatments*

Parameter	*Surgically treated*	*Non-surgically treated*	*p-value*
ATRS No. of patients Mean ± SD	 12 92.4 ± 7.1	 9 74.3 ± 28.2	 0.069
Heel-rise height No. of patients Mean ± SD	 11 84.0 ± 10.5	 9 73.7± 8.5	 ***0.037***
Heel-rise work No. of patients Mean ± SD	 11 79.6 ± 13.6	 8 58.2 ± 16.1	 ***0.01***
CMJ No. of patients Mean ± SD	 12 94.4 ± 13.4	 9 84.0 ± 17.8	 0.394
Hopping No. of patients Mean ± SD	 12 103.8 ± 18.6	 9 94.6 ± 58.6	 0.227

CONCLUSION

Acute US measurement showing the diastasis between the ruptured tendon ends may give the treating physician an indication of the risk of sustaining a re-rupture and a poor outcome, thereby providing guidance in the decision-making between surgical and non-surgical management. The non-surgical management of Achilles ruptures with a gap of > 10 mm had a significantly higher rate of re-rupture than non-surgical treatment with a gap of < 10 mm. The non-surgical management of ruptures with a gap of > 5 mm led to inferior outcomes for heel-rise height and heel-rise work compared with surgical treatment.

12.2 STUDY II

Longer duration of operative time enhances healing metabolites and improves patient-reported outcome after Achilles tendon rupture surgery

INTRODUCTION

The relationship between the duration of operative time, healing response and patient outcome has not previously been investigated. An enhanced healing response related to the DOT may potentiate repair processes, especially in hypovascular and sparsely metabolised tendons.

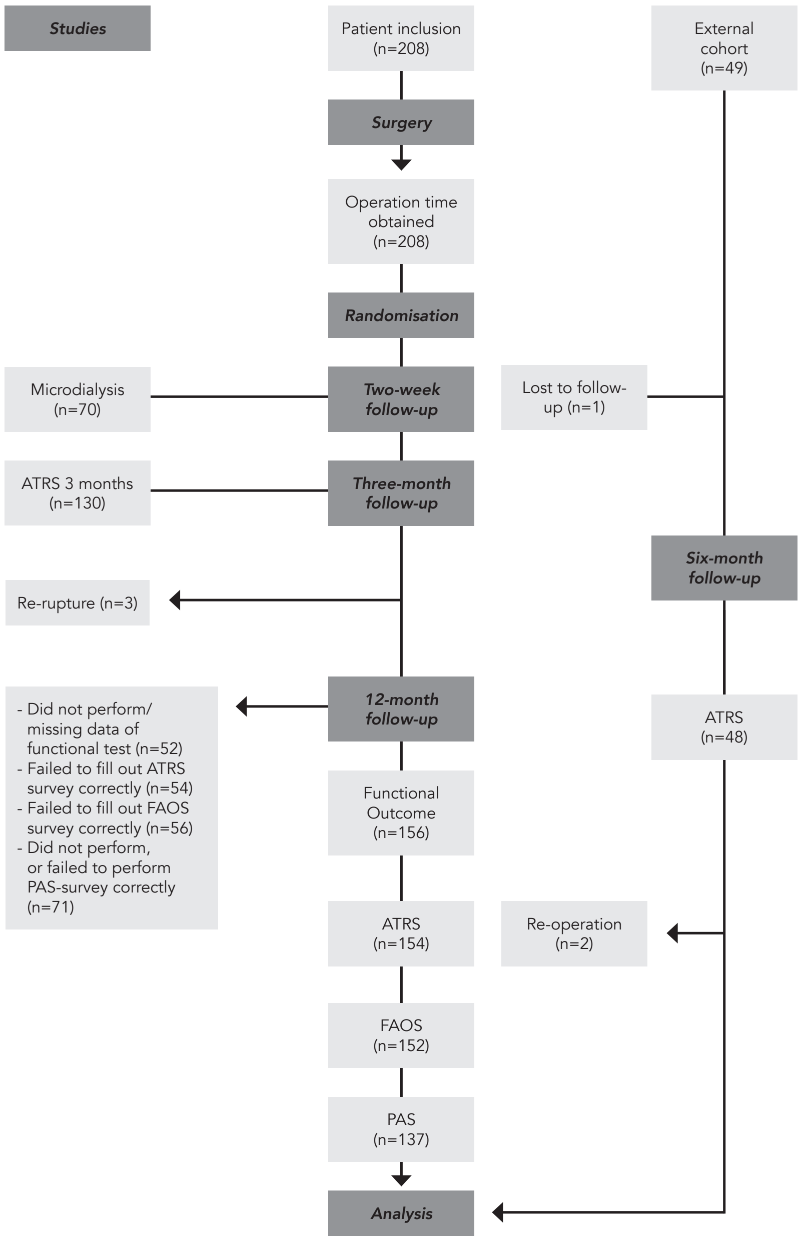
PURPOSE

This study aimed to investigate the association between the DOT and the metabolic healing response, patient-reported outcome and the rate of postoperative complications after acute Achilles tendon injury.

METHODS

An observational cohort, cross-sectional study with observers blinded to patient grouping. A total of two hundred and fifty-six prospectively randomised patients (210 men, 46 women; mean age 41 years (SD 9 years) with an acute total Achilles tendon rupture all operated on using a uniform surgical technique were assessed retrospectively. At two weeks postoperatively, six metabolites were quantified using microdialysis. At three, six and 12 months, patient-reported pain, walking ability and physical activity were examined using self-reported questionnaires, the ATRS, the foot and ankle outcome score and the physical activity scale. At 12 months, functional outcome was assessed using the heel-rise test. Complications, such as deep venous thrombosis, infections and re-operations, were recorded throughout the study. A flow chart of the study is shown in figure XVIII.

Figure XVIII. *Flow chart of the study*



RESULTS

Patients who had a longer DOT exhibited higher levels of glutamate (p = 0.026) and glycerol (p = 0.023) at two weeks. At the one-year follow-up, a longer DOT was associated with significantly less loss of physical activity (p = 0.003), less pain (p = 0.009), fewer walking limitations (p = 0.022) and better functional outcome (p = 0.014). The DOT did not correlate significantly with the rate of adverse events, such as deep venous thrombosis, infections or re-ruptures. Higher glutamate levels were associated with less loss of physical activity (p = 0.017). All correlations were confirmed by multiple linear regressions taking confounding factors into consideration. In Table VII, the outcome is dichotomised after the median operative time, as long and short operations and how the outcomes in the study vary between the two groups.

CONCLUSION

The results of this study suggest a previously unknown mechanism, indicating an increased metabolic response associated with a longer DOT, which may improve tendon healing and patient-related outcome after Achilles tendon rupture surgery. Allowing for a larger amount of traumatised tissue, as reflected by the upregulation of glycerol in patients with a longer DOT, may prove to be an important surgical aspect of the stimulation of repair of hypometabolic soft-tissue injuries, such as Achilles tendon ruptures.

Table VII. Results of patients divided by duration of operative time

Outcomes	***≤34 min Mean (SD)***	***>35min Mean (SD)***	***p-value***
Two weeks – Metabolites			
Glucose	2.72 (0.76)	2.71 (0.74)	0.924
Lactate	1.75 (0.73)	1.59 (0.89)	0.468
Pyruvate	90.65 (24.89)	89.13 (29.33)	0.826
Glycerol	62.88 (22.72)	107.84 (106.36)	***0.014***
Glutamate	78.35 (30.44)	84.50 (32.72)	0.471
Lactate-pyruvate ratio	19.12 (5.14)	18.56 (6.56)	0.727
Three months – Patient-reported			
Pain (ATRS)	6.57 (3.03)	7.46 (2.02)	***0.048***
Walking limitations (ATRS)	5.09 (2.61)	5.63 (2.58)	0.244
*Six months – Patient-reported **			
Pain (ATRS)	8.25 (1.75)	8.17 (2.25)	0.897
Walking limitations (ATRS)	8.00 (1.69)	9.00 (1.09)	***0.021***
12 months – Patient-reported			
Pain (ATRS)	8.51 (2.28)	9.18 (1.49)	***0.016***
Walking limitations (ATRS)	8.40 (2.03)	9.19 (1.35)	***0.006***
Pain (FAOS)	92.86 (10.37)	96.15 (6.88)	***0.025***
Change in Physical Activity Level	1.05 (0.96)	0.49 (1.02)	***0.001***
12 months – Functional			
Number of heel rises - Injured side	24.01 (8.82)	25.93 (7.80)	0.172
Number of heel rises - Uninjured side	29.59 (8.97)	30.78 (8.23)	0.651
Limb Symmetry Index - Repetitions	0.83 (0.23)	0.86 (0.20)	0.240

Abbreviations: ATRS=Achilles tendon Total Rupture Score; FAOS=Foot and Ankle-Outcome Score; PAS=Physical Activity Scale. *= Separate data from the external cohort and therefore dichotomised by separate median duration of operative time of <42 minutes and ≥42 minutes.
The outcome variables are dichotomised into two groups (short and long operative time) by the median operative time. Bold indicates a significant p-value less than 0.05. The dichotomised data of the metabolite glutamate and the functional outcome are in contrast to the multiple regression analyses, not significantly different between the groups.

12.3 STUDY III

Patients with an Achilles tendon re-rupture have long-term functional deficits and a poorer patient-reported outcome than those with primary ruptures

INTRODUCTION

Achilles tendon re-rupture is a dreaded complication. In view of this, the focal point of much Achilles tendon research has been to prevent re-rupture. However, very little is known about its long-term outcome and how it differs from primary ruptures.

PURPOSE

The aim of this study was to perform a long-term follow-up of patients treated for an Achilles tendon re-rupture, using established outcome measurements for lower extremity function and symptoms, and to compare the results with those on the uninjured side. A secondary aim was to compare the outcome with that of patients treated for primary ruptures.

METHODS

Twenty patients (four females) with a mean (SD) age of 44 (10.9) years, ranging from 24 to 64, were included. The patients were identified by reviewing the medical records of all Achilles tendon ruptures at Sahlgrenska University Hospital and Kungsbacka Hospital, Sweden, between 2006 and 2016. All patients received standardised surgical treatment and rehabilitation. The mean (SD) follow-up was 50.9 (38.1) months. A test battery of validated clinical and functional tests, patient-reported outcome measurements and measurements of tendon elongation were performed at the final follow-up. This cohort was then compared with the two-year follow-up results from a previous randomised controlled trial of patients treated for primary Achilles tendon rupture[136].

RESULTS

There were deficits on the injured side compared with the healthy side in terms of heel-rise height (11.9 versus 12.5 cm, p = 0.008), repetitions (29 versus 32 p = 0.004) and drop-jump height (13.2 versus 15.1 cm, p = 0.04). There was a significant difference in calf circumference (37.1 versus 38.4 cm, p =0.001) and ankle dorsiflexion on the injured side compared with the healthy side (35.3 versus

40.8 degrees, p =0.003). However, no significant differences were found in terms of tendon length, 22.5 (2.5) cm on the injured side and 21.8 (2.8) cm on the healthy side. Compared with primary ruptures, the re-rupture cohort obtained significantly poorer results for the ATRS, with a mean of 78 (21.2) versus 89.5 (14.6) points (p =0.007) respectively. The re-ruptures showed a higher mean LSI heel-rise height, 94.7% (9.3%) versus 83.5% (11.7%) (p = < 0.0001), and superior mean LSI eccentric-concentric power, 110.4% (49.8%) versus 79.3% (21%) (p = 0.001), than the primary ruptures.

Table VIII. Results for re-ruptures compared with primary ruptures

	Re-rupture (n=20)	*Primary rupture (n=81)*	*p-value*
Patient-reported outcome			
ATRS	78.0 (21.2) (68.1; 87.9) n = 20	89.5 (14.6) (86.3; 92.7) n = 81	***0.007***
PAS	3.90 (1.17) (3.35; 4.45) n = 20	3.76 (0.95) (3.55; 3.96) n = 81	n.s
Functional outcome			
Heel Rise Work	86.2 (29.1) (72.2; 100.2) n = 19	81.2 (18.6) (77.1; 85.3) n = 80	n.s
Heel Rise Rep	88.0 (18.6) (79.0; 97.0) n = 19	97.7 (16.7) (94.0; 101.5) n = 80	n.s
Heel Rise Height	94.7 (9.3) (90.4; 99.1) n = 20	83.5 (11.7) (80.9; 86.1) n = 80	***<.0001***
CMJ	94.7 (17.6) (86.4; 102.9) n = 20	91.9 (14.8) (88.6; 95.2) n = 81	n.s
Concentric power	93.5 (38.9) (75.3; 111.7) n = 20	86.1 (32.9) (78.7; 93.4) n = 79	n.s
Eccentric-concentric power (W)	110.4 (49.8) (86.4; 134.4) n = 19	79.3 (21.0) (74.5; 84.0) n = 78	***0.001***
Drop CMJ	89.2 (22.3) (78.8; 99.6) n = 20	88.7 (16.3) (85.1; 92.3) n = 80	n.s

For continuous variables, the mean (SD)/(95% CI for mean)/n= is presented.
CMJ= Counter Movement Jump
DJ= Drop jump
ATRS = Achilles Tendon Total Rupture Score
PAS= Physical Activity Scale

Table IX. Results for injured versus healthy side

			Comparison between injured side and healthy side		
	Injured side (n=20)	***Healthy side (n=20)***	***Mean difference***	***Effect size***	***p-value***
Hopping height (cm)	4.13 (1.73) (3.32; 4.94) n = 20	4.11 (1.92) (3.21; 5.01) n = 20	-0.02 (0.99) (-0.48; 0.48) n = 20	0.01	n.s
Hopping Polymetric quotient	0.53 (0.14) (0.47; 0.6) n = 20	0.54 (0.18) (0.46; 0.62) n = 20	0.01 (0.1) (-0.04; 0.05) n = 20	0.03	n.s
CMJ height (cm)	12.6 (5.3) (10.1; 15.1) n = 20	13.5 (5.1) (11.1; 15.8) n = 20	0.88 (2.67) (-0.37; 2.12) n = 20	0.17	n.s
Drop CMJ (cm)	13.2 (5.5) (10.7; 15.8) n = 20	15.1 (6.3) (12.2; 18.1) n = 20	1.90 (4.12) (-0.03; 3.83) n = 20	0.32	***0.039***
Concentric power (W)	301.9 (181.8) (216.8; 387.0) n = 20	319.3 (227.6) (212.8; 425.8) n = 20	17.4 (147.6) (-51.7; 86.5) n = 20	0.08	n.s
Eccentric-concentric power (W)	368.0 (231.4) (256.4; 479.5) n = 19	322.5 (133.2) (260.2; 384.8) n = 20	-33.8 (182.9) (-121.9; 54.4) n = 19	0.24	n.s
Heel-rise repetitions(n)	28.5 (14.0) (21.7; 35.2) n = 19	31.7 (12.6) (25.7; 37.8) n = 19	3.26 (4.63) (1.03; 5.49) n = 19	0.24	***0.004***
Heel-rise work (J)	1960 (830) (1560; 2370) n = 19	2320 (770) (1950; 2690) n = 19	360 (660) (40; 680) n = 19	0.45	n.s
Heel-rise height (cm)	11.9 (1.9) (11.0; 12.7) n = 20	12.5 (1.5) (11.8; 13.3) n = 20	0.68 (1.22) (0.11; 1.24) n = 20	0.35	***0.0078***

For continuous variables, the mean (SD)/(95% CI for mean)/n= is presented.
CMJ= Counter Movement Jump

12.4 STUDY IV

Cost-effectiveness analysis of the surgical versus the non-surgical management of acute Achilles tendon ruptures

INTRODUCTION

An Achilles tendon rupture is a common injury that typically affects people in the middle of their working lives. The injury has a negative impact in terms of both morbidity for the individual and the risk of substantial sick leave.

PURPOSE

The aim of this study was to investigate the cost-effectiveness of the surgical compared with the non-surgical management of patients with an acute Achilles tendon rupture.

METHODS

One hundred patients (86 men, 14 women; mean age, 40 years SD 9.2 years) with an acute Achilles tendon rupture were randomised (1:1) to either surgical treatment or non-surgical treatment, both with an accelerated rehabilitation protocol (surgical; n = 49, non-surgical; n = 51) figure XIX. One of the patients in the surgical group was excluded due to a partial re-rupture and five patients in the same group were lost to the one-year economic follow-up. One patient was excluded due to incorrect inclusion and one was lost to the one-year follow-up in the non-surgical group. The cost was divided into direct and indirect costs. The direct cost is the actual cost of health care, whereas the indirect cost is the production loss related to the impact of the patient's injury in terms of lost ability to work. The health benefits were assessed using quality-adjusted life years. Sampling uncertainty was assessed by means of non-parametric bootstrapping.

RESULTS

Pre-injury, the groups were comparable in terms of demographic data and health-related quality of life, Table X. The mean cost of surgical management was €7,332 compared with €6,008 for non-surgical management (p = 0.024). The mean number of QALYs during the one-year time period was 0.89 and 0.86 in the surgical and non-surgical groups respectively. The (incremental) cost-effectiveness ratio was €45,855. Based on bootstrapping, the cost-effectiveness acceptability curve shows that surgical treatment is 57% likely to be cost-effective at a threshold value of €50,000 per QALY, figure XX.

Figure XIX. Flow chart of the study

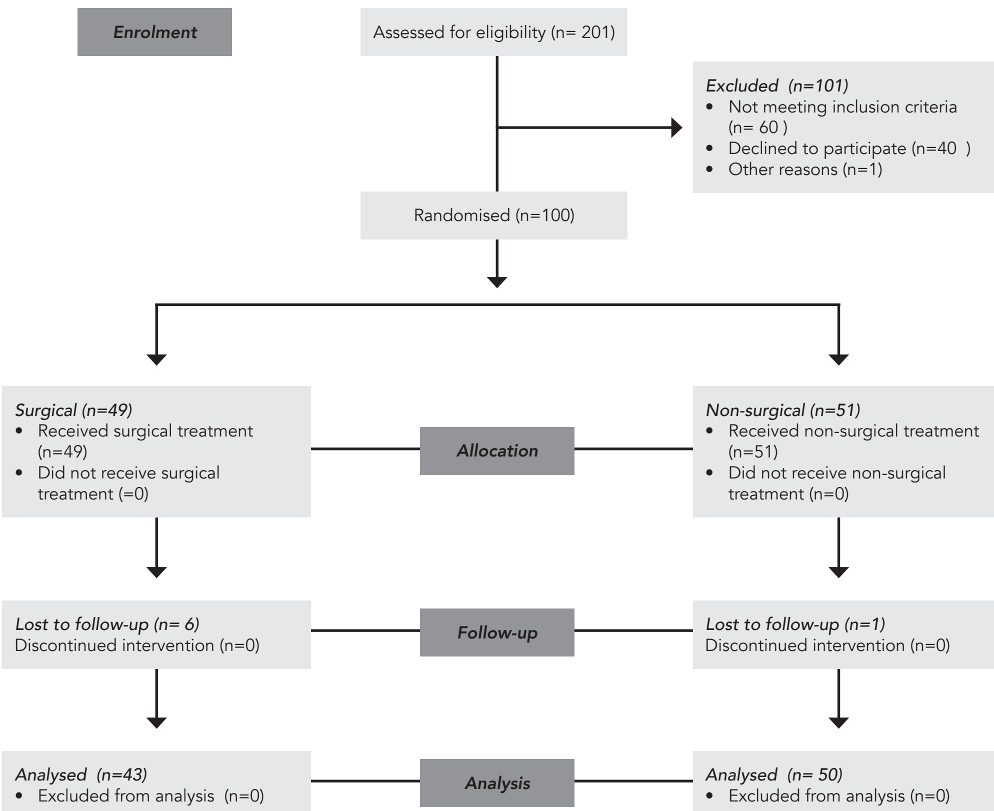


Table X. Results of surgical versus non-surgical treatment

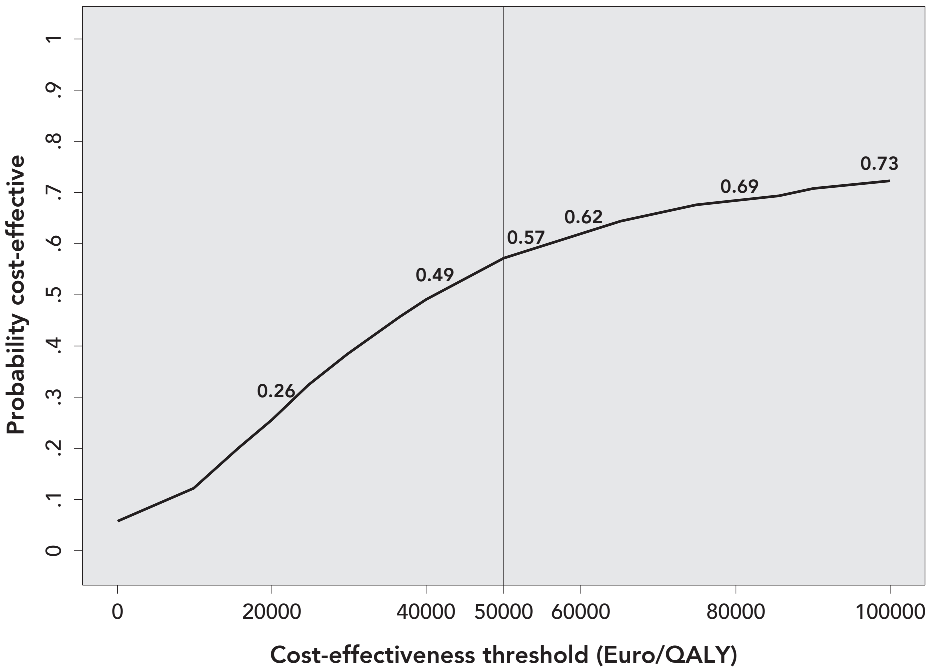
	Total (n=93)	*Surgical (n=43)*	*Non-surgical (n=50)*	*p-value*
Gender				
Male	80 (86.0%)	34 (79.1%)	46 (92.0%)	
Female	13 (14.0%)	9 (20.9%)	4 (8.0%)	0.14
Age	39.3 (9.2)	38.9 (8.7)	39.7 (9.7)	0.68
Income (euros/month)	3711 (1563)	3505 (1560)	3887 (1561)	0.24
Re-rupture				
Yes	6 (6.5%)	1 (2.3%)	5 (10.0%)	
No	87 (93.5%)	42 (97.7%)	45 (90.0%)	0.28
Hospital admission				
Yes	5 (5.4%)	3 (7.0%)	2 (3.8%)	
No	88 (94.6%)	40 (93.0%)	51 (96.2%)	0.53
# Visit to doctor	4.31 (1.62)	4.79 (1.15)	3.90 (1.85)	0.099
# Physio visits	26.6 (13.2)	28.2 (13.1)	25.3 (13.3)	0.29
# Sick days	21.2 (25.5)	17.8 (19.0)	24.1 (29.9)	0.24
Direct cost	3869 (1704)	5 007 (1009)	2890 (1571)	***<0.001***
Indirect cost	3073 (3833)	2 675 (3365)	3416 (4198)	0.36
Total cost	6942 (4116)	7 682 (3621)	6305 (4435)	0.10

Notes: For categorical variables, n is presented and, for continuous variables, the mean (standard deviation). P-values based on the null hypothesis of equal proportions (dichotomous variables) and means (continuous variables) using large-sample equal proportions test and t-tests respectively.

CONCLUSION

Surgical treatment was more expensive compared with non-surgical management, i.e. the direct costs were significantly higher (73%) (p>0.001), and there were no statistically significant differences between treatments in terms of indirect and total costs. The cost-effectiveness results provide weak support (57% likelihood) for surgical treatment being cost-effective at a willingness to pay per QALY threshold of €50,000. This represents support for surgical treatment; however, additional cost-effectiveness studies together with RCTs are important to clarify which treatment option is preferred from a cost-effectiveness perspective.

Figure XX. Cost-effectiveness acceptability curve



12.5 STUDY V

Mapping functions in health-related quality of life: mapping from the Achilles Tendon Total Rupture Score to the EQ-5D

INTRODUCTION

Health economics is a rapidly expanding field, as more pressure is imposed on physicians to justify their treatments. The standard method for calculating quality-adjusted life years is to use the EQ-5D. Unfortunately, this patient-reported outcome is not regularly used in Achilles tendon research. It is therefore of interest to perform a mapping study that is able to convert the ATRS into the EQ-5D score in order to be able to use the ATRS in health-economic evaluations.

PURPOSE

Health-state utility values are derived from preference-based measurements and are useful in calculating quality-adjusted life years, which is a metric commonly used in cost-effectiveness studies. The purpose of this study was to convert the ATRS to the preference-based European Quality of Life-5 Dimension Questionnaire by estimating the relationship between the two scores using mapping.

METHODS

Data were collected from a randomised controlled trial, where 100 patients were treated either surgically or non-surgically for an Achilles tendon rupture. Forty-three and 44 patients in the surgical group and non-surgical groups, respectively completed the ATRS and the EQ-5D alongside each other during follow-up at three time points. Different models of the relationship between the ATRS and the EQ-5D were developed and analysed based on direct mapping and cross-validation. The model with the lowest mean absolute error was observed as the one with the best fit.

RESULTS

Among the competing models, mapping based on using a combination of the ATRS items four, five, and six, associated with limitation due to pain, during activities of daily living and walking on uneven ground, produced the best predictor of the EQ-5D score.

Table XI. Results from model E

Variable	*OLS coefficients (std.err.)*	*Multilevel model coefficients (std.err.)*
ATRS Item 4	0.0189* (0.0040)	0.0183* (0.0030)
ATRS Item 5	0.0181* (0.0045)	0.0158* (0.0044)
ATRS Item 6	0.0119* (0.0036)	0.0129* (0.0038)
Constant	0.4784* (0.0400)	0.4936* (0.0213)
Var (Constant)[a]	-	0.0016* (0.0009)
R^2	0.57	-

p >0.001
[2] Variance of constant

CONCLUSION

Utility values are best obtained directly using preference-based measurements, while deriving them with mapping is an alternative solution in clinical trials where only non-preference-based measurements are available. In this study, a mapping algorithm between the ATRS and the EQ-5D was developed, thereby providing a way to perform QALY-based cost-effectiveness analyses of acute Achilles tendon rupture treatment.

12.6 STUDY VI

Patient predictors of one-year patient-reported and functional outcome after acute Achilles tendon rupture – multicentre studies of 391 patients

INTRODUCTION

Recent research on Achilles tendon ruptures has focused on the individualisation of treatment. In order to guide the treating health-care professional, predictions of outcome are important. Previous predictor studies have produced conflicting results and have included a small number of patients.

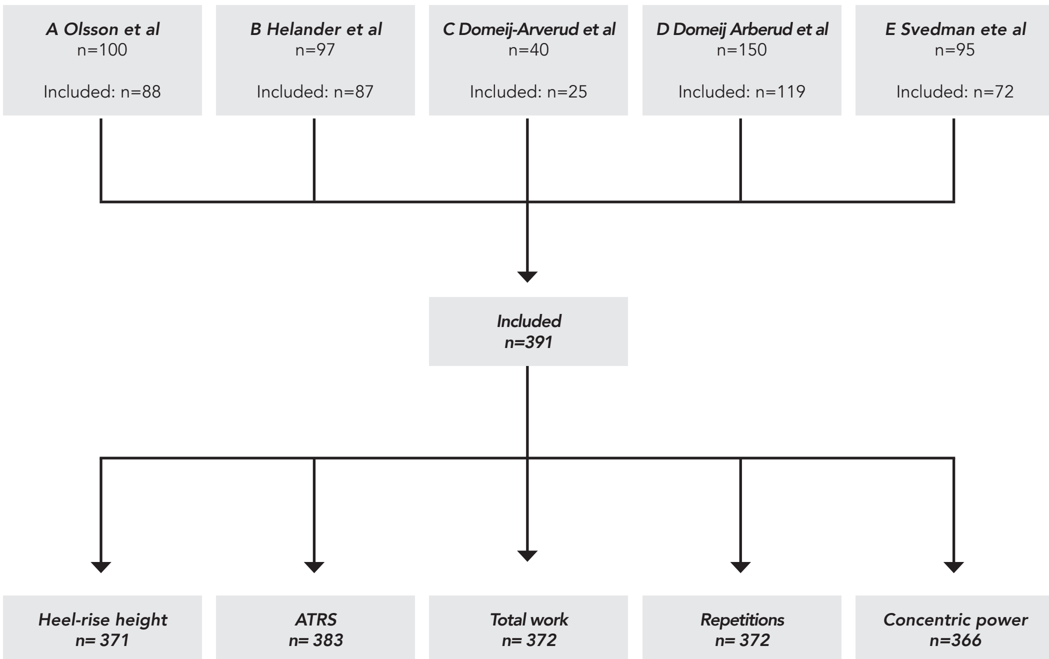
PURPOSE

To determine the predictors of functional and patient-reported outcome one year after an acute Achilles tendon rupture, using a multicentre cohort, and to determine patient characteristics for reporting in the best and worst ten percentiles of the Achilles tendon total rupture score and heel-rise test. The hypothesis was that older age, higher body mass index and female gender are predictors to inferior outcomes.

METHODS

The patients were included by combining five randomised controlled trials from two different centres in Sweden. The functional outcome was assessed using the validated heel-rise tests (height, repetitions, total work and concentric power) for muscular endurance and strength and the relationship between the injured and uninjured leg was calculated as the limb symmetry index. Patient-reported outcome was measured using the ATRS. All outcomes were collected at the one-year follow-up. Independent predictors included in the analysis were patient gender, current smoking, body mass index and surgical versus non-surgical treatment.

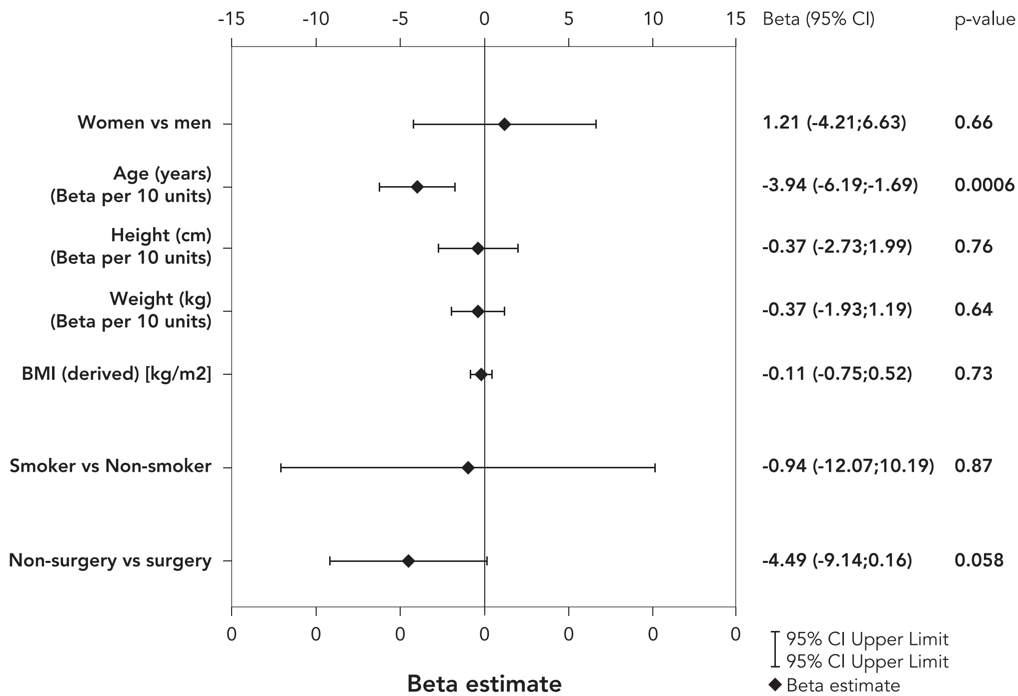
Figure XXI. Flow chart of the study



RESULTS

Of the 391 included patients, 309 (79%) were treated surgically, figure XXI demonstrates a flowchart of the study. The LSI of heel-rise height at the one-year follow-up decreased by approximately 4% for every 10-year increment in age (beta = -3.94 (95% CI; -6.19;-1.69), (p = 0.0006), figure XXII. In addition, every 10-year increment in age resulted in a 1.79-fold increase in the odds of being in the lowest 10 percentiles of the LSI heel rise. Moreover, a non-significant superior LSI for heel-rise height was found in patients treated with surgery compared with non-surgical treatment (beta= -4.49 (95 % CI; -9.14; 0.16), (p = 0.058). No significant predictor was found for the ATRS. Current smoking, patient gender and body mass index did not significantly affect the one-year results for the LSI of the heel-rise tests.

Figure XXII. Diagram of predictors of outcome for LSI heel-rise height



CONCLUSION

Older age at the time of injury negatively affects heel-rise height one year after an Achilles tendon rupture. Irrespective of age, a tendency towards the superior recovery of heel-rise height was seen in patients who were treated surgically. None of the studied factors affected patient-reported outcome.

13 DISCUSSION

13.1. PREDICTORS

13.1.1. ACUTE ULTRASOUND INVESTIGATION

THE TWO TRADITIONAL GOALS OF ACHILLES TENDON RESEARCH ARE:
TO IMPROVE OUTCOME AND
TO AVOID RE-RUPTURES.

In order to achieve this, we require a better understanding of the factors that predict functional outcome and how we can use them to individualise treatment in the most effective manner. Imaging that can be used to measure the gap in the injured tendon in the acute setting is an interesting and potentially important instrument and is currently not used in the routine management of patients with an Achilles tendon rupture.

Previous research has indicated that a gap of more than five mm indicates mechanical failure[95]. It is also likely that most re-ruptures occur due to the fact that the tendon has not healed completely and, when treatment with the lower leg brace is discontinued, the tendon ruptures again as a result of only minor trauma. Voleti et al.[176] have shown that, if there is insufficient tendon contact in the early phase, a healing problem or non-healing can be expected. However, tendon healing is similar to bone healing, with new tendinous tissue forming a callus to bridge the gap between the tendon ends. To be able to restore the continuum, the ends need proximity, as strength and other mechanical properties continuously improve during the healing phase[99]. All of this indicates that, the gap size is of major importance. The accurate and reliable measurement of gap size may therefore be crucial to the treatment of a ruptured Achilles tendon.

The purpose of both management strategies, i.e. surgical and non-surgical protocols, is to move the ruptured tendon ends into apposition, which can be achieved either by suturing the ends together or by placing the foot in plantar flexion (non-surgical treatment). One of the most important findings in Study I was that all the identified re-ruptures were in the >5 mm group (>10 mm subgroup) and were treated non-surgically. The total number of patients in this subgroup was four, three of whom sustained a re-rupture. This gives a positive predictive value of 75% for sustaining a re-rupture with an initial gap of >10 mm and being treated non-surgically. These results indicate that patients with a large initial gap diastasis would benefit from surgical treatment in order to avoid a re-rupture. This finding is in harmony with previous studies[85, 171]. Interestingly, the patients that had a diastasis of more than five mm and were treated non-surgically had a significantly poorer patient-reported outcome, lower heel-rise height and trend towards lower heel-rise work. This in turn would suggest an inferior outcome. It is important to note that there is considerable uncertainty in these results, as the study population is small and some uncertainty in the ultrasound method is likely, as the kappa coefficient is missing.

These results support the hypothesis that the size of the diastasis might be used as a measurement to determine the need for surgical treatment, but further research is needed to confirm whether five mm is the optimal cut-off. The reason why ultrasonography is not used more frequently is most probably that it is highly user dependent and, accordingly, there might be a high risk of false negatives, together with the fact that a clinical diagnosis is regarded as valid and reliable to establish the diagnosis[105]. However, as advances in medical imaging are taking place rapidly, it may well be that the next generation of ultrasonography will be better and more accessible, which would make it easier to implement in routine patient care.

Magnetic resonance imaging has also been shown to be a useful tool for assessing the diastasis between the ruptured tendon ends[78]. However, higher costs and poorer accessibility are currently restricting its use. With future development within the field of radiology and with more readily available MRI scans, it appears that MRI could play a more important role in the future when assessing rupture patterns. Comparing patients that had a diastasis of more than five mm and were treated surgically and non-surgically, the heel-rise test showed superior results for the surgically treated group. This may be due to less elongation of the tendon in the surgical group; however, as stated previously, this has not yet been demonstrated in research.

Main result

Acute ultrasonography investigation could be a useful tool for predicting the risk of re-rupture as well as outcome.

13.1.2. DURATION OF OPERATIVE TIME

Duration of operative time and how it correlates with functional outcome is an area that is not well understood. There are relatively few publications in this field and there are no previous publications on the topic of Achilles tendon injuries. The time an operation takes is always of great interest, for both the patient and the surgeon.

Previous publications relating to bariatric surgery have reported a higher rate of adverse events, such as deep venous thrombosis and a prolonged hospital stay, when surgical time is prolonged[29]. However, there are some previous studies that suggest that a longer surgical time might result in fewer re-operations[32, 175]. This thesis demonstrates that patients with a longer duration of surgery indicated a better outcome in terms of physical activity compared with a shorter duration of surgery, when dichotomised into two groups based on the median operative time. Patients with a long duration of surgery only experienced half the reduction in terms of the physical activity scale compared with the short duration. This equals one step on the PAS score, e.g. from four to three, which in practice means "gardening for one to two hours a week", instead of "hard physical labour" for construction work. A difference like this could be considered to be clinically relevant and can potentially lead to improved health for these patients[44].

13.1.3. HEALING METABOLITES

Knowledge of healing metabolites is an emerging field within Achilles tendon research and it can hopefully be used in the future as an instrument for predicting patient-reported outcome and help researchers to understand why some tendons heal well with good function while others do quite the opposite. This thesis show that, with a longer DOT, there was an upregulation of glutamate and glycerol. Elevated levels of glycerol indicate increased trauma, as it is a marker of cell breakdown[48, 115]. With a longer duration of surgical time, it is likely that the tissues will undergo more trauma, resulting in a greater degree of cell damage, compared with a faster, less invasive procedure. Increased glycerol levels may also suggest a general upregulation of the growth factor synthesis[122].

Glutamate is the other upregulated metabolite that was correlated to a longer DOT. In contrast to glycerol, glutamate is involved in enhancing the healing process in tendon healing[153, 174]. This upregulation gives strength to the finding that a longer DOT leads to improved healing, which will in turn lead to improved function. Glutamate works in several different ways to aid healing; the chemotaxis of neutrophils[60], improved angiogenesis, cell proliferation and nerve ingrowth[153]. It is also worth noting that the increased level of glutamate was significantly associated with an improved patient-reported outcome, which could potentially be related to this increased level of glutamate.

Main result

A longer duration of surgery leads to the upregulation of healing metabolites.

13.1.4. PATIENT-RELATED PREDICTORS OF OUTCOME

In order to be able to give better advice to patients and better individualise treatment, it is important to understand how the patients' characteristics are able to predict the outcome. This thesis presents the largest predictor study to date within this field and helps to clarify the contradictory results from previous studies. The strongest predictor of a poorer one-year functional outcome has been shown to be older age at the time of injury; the odds of achieving a more symmetrical heel rise become progressively poorer with increasing age at the time of injury. There was also a non-significant relationship for surgically treated patients to experience a greater recovery in heel-rise height in comparison with non-surgically treated patients. No differences in functional or patient-reported outcome could be identified between the sexes or in patients with a higher BMI.

These results are in line with previous predictor models[7, 137]. The decrease in heel-rise height found among older patients may be explained by degenerative changes related to age and changes in collagen synthesis leading to increased stiffness[180]. Mechanisms that are suggested to contribute to tendon change with age are the formation of advanced glycation end-product crosslinks, an ageing stem cell population, reactive oxygen species and cellular senescence[12].

Age is a non-modifiable risk factor and it is a demonstrated here as a strong predictor of inferior heel-rise height, but it was not able to predict a poorer outcome in the other functional test or ATRS. It is possible that, as patients age, their functional expectations decrease and they would therefore report a better patient-reported outcome than might otherwise be the case. These findings are important in clinical practice and age is a factor to consider when developing a treatment algorithm for these patients, including surgical repair and rehabilitation.

The question of whether gender is able to predict a poorer or a better outcome is interesting and there is disagreement in previous publications[7, 137, 159]. The reason for this is probably due to the fact that it is relatively rare for females to sustain Achilles tendon rupture and it has therefore been difficult to include large number of patients in previous studies. In this model, we included 57 women, which, to our knowledge, is the strongest to date. We were unable to show that gender predicts outcome in any of the four tested variables, nor did it influence the analyses of superior or inferior outcome. This is an important finding, as it can provide an insight into why previous studies are conflicting and the fact that gender should not be regarded as a predictor of functional or subjective outcome.

Current smoking is fortunately very rare in patients with an Achilles tendon injury and this is due to the fact that it mainly affects active men between the age of 35-45 and the prevalence of smoking in this group is very low. The downside is that we were only able to include 16 smokers in the analysis. The fact that smoking is bad for human beings in almost every respect is well known and it has been shown to be a predictor of poorer outcome in numerous orthopaedic conditions, such as spine surgery and rotator cuff repair[54, 72, 150]. Surprisingly, smoking did not emerge as a negative predictor in any of the tested variables, but this is probably due to the limited cohort that was tested. It would be of great interest to include more smokers in a similar model. Body mass index is another factor that predicted a poorer outcome at six and 12 months in the study by Olsson et al.[137]. However, this thesis is unable to provide support for that finding. On the contrary, BMI was not found to be a significant predictor.

Another finding worthy of note from this thesis is that patients treated surgically had a clear trend towards a more symmetrical heel-rise height compared with non-surgically treated patients. Silbernagel et al.[163] reported a significant relationship between tendon elongation and heel-rise height, with more elongation of the tendon, the lower the heel-rise height. So this finding could provide further evidence for the assumption that surgically treated patients have less elongation and accordingly a greater LSI heel-rise height. If surgery is able to predict better heel-rise height, it may then be important for patients with high physical demands to be surgically treated in order to maximise the chance of optimal recovery. In predictor analyses, several hypotheses are tested in order to see if there is a significant difference. With this method of testing, there is always a risk of mass significance that needs to be considered when interpreting the results.

Main result

Older age at the time of injury is a strong predictor of negative outcome.

13.2. RE-RUPTURES

13.2.1. LONG-TERM OUTCOME OF RE-RUPTURES

Re-rupture is one complication that needs to be avoided, as it can be equated with complete failure of treatment. As we will be able to find predictors that may help physicians to avoid this dreaded complication, it is also of great interest to know more about these patients' long-term outcome and how re-ruptures compare with primary ruptures. The most important finding relating to re-ruptures presented in this thesis is the fact that this group is significantly affected by their injury years after active rehabilitation has finished. Patient-reported outcome scores were low in terms of both ATRS and FAOS scores and only two patients reported full recovery. Functional deficits were more frequently present on the injured side compared with the healthy side and in comparison with patients who had sustained primary ruptures; patients with a re-rupture had poorer patient-reported outcomes. However, and surprisingly, patients treated for a re-rupture had similar or even superior results in functional tests.

There is also a relationship between the subjective complaints and functional outcome. In comparison, the heel-rise height was poorer on the injured side compared with the healthy side. Previous studies have shown reduced plantar flexion strength after a re-rupture[139, 142]. However, in contrast, Metz et al.[119] did not find any such deficits in strength. It has been postulated that this difference was due to the differences in follow-up period, with Metz et al. reporting a mean follow-up of nine years. However, a seven-year follow-up of primary ruptures recently published by Brorsson et al.[19] contradicts this and shows that no significant recovery occurs after the first two years.

Moreover, significant functional deficits were found in terms of heel-rise repetitions, heel-rise height and drop CMJ compared with the healthy side. The largest difference between the injured and healthy sides was found in heel-rise work, but the effect size indicates that the differences are still minor. It is clear that, in most patients, re-ruptures will lead to an inferior functional outcome for the injured tendon compared with the healthy tendon and that there is a large variation between patients. This indicates that some patients recover well, whereas others make an unsatisfactory recovery. A similar picture is found for patients with primary ruptures. The reasons need to be further explored.

To understand how the re-ruptures compared with primary ruptures, they were compared with patients' two-year follow-up data from a previous RCT[136] comparing surgical and non-surgical treatments. It was recently shown that no significant improvement in terms of function occurs after two years[17] and we therefore concluded that this comparison would reflect the long-term outcome for primary ruptures. Interestingly, the re-rupture group had a poorer patient-reported outcome, but the functional outcome was very similar or even superior in terms of heel-rise height and eccentric power. As heel-rise height is a reflection of the length of the tendon[75], this possibly shows that the surgical technique used for the re-rupture group is superior when it comes to maintaining the length of the tendon compared with the treatment protocols for the primary ruptures. The FAOS score showed that re-ruptures obtain poor quality-of-life scores compared with primary ruptures, indicating that patients who have sustained a re-rupture are severely affected by their injury. The poorer patient-reported outcome is probably due to the severity of the injury and the prolonged psychological impact, as it is not reflected in the functional outcome. Patients with re-ruptures may require closer contact with their physiotherapist to improve the functional outcome and their quality of life during the follow-up period.

Main result

Patients who have sustained a re-rupture have lasting long-term deficits in function compared with the healthy side.

Main result

Patients who have sustained a re-rupture have a poorer patient-reported outcome compared with primary ruptures, although similar to superior functional outcome.

13.3. ECONOMIC IMPACT

13.3.1. COST

Calculating the total cost of both surgically and non-surgically managed Achilles tendon ruptures is a challenging, yet important task. As health care costs are increasing, increased pressure is continually being placed on surgeons to be able to defend the cost of their intervention. This is especially essential in orthopaedics, where there is often a choice between surgical and non-surgical treatment[13, 61, 173]. There are numerous different variables to take into account and to facilitate this, the costs need to be discussed in terms of direct and indirect costs.

The total cost was higher for the surgically treated group. This was due to the cost that was associated with the surgical procedure itself. The mean SD cost for the surgical procedure in this thesis was 1,805 (432) euros. This is in line with the cost-minimisation analysis conducted by Truntzer et al.[173]. In terms of indirect costs, the number of sick-leave days was higher in the non-surgical group, which is in agreement with what Möller et al.[120] previously described. The reason for this is the five re-ruptures in the non-surgical group, which had a mean sick leave of 26.8 (12) days. There is a large variation between patients when it comes to time off work. This variation in production loss is related to several factors. The first is the type of occupation. Patients with a physical job such as builders will naturally have a longer time off work compared with an office worker. Another factor is insurance, as some employers may not allow their employee to work while wearing a brace. Lastly, socioeconomic factors are of importance; some people may simply not be able to afford not to work.

Main result

It is more expensive to treat an Achilles tendon rupture surgically compared with non-surgically.

13.3.2 COST-EFFECTIVENESS

The cost per QALY for surgical versus non-surgical treatment presented in this thesis is 45,855 euros. This means that the decision-maker will have to pay 45,855 euros per QALY gained. This cost can be compared with the Swedish National Board of Health and Welfare that quotes 50,000 euros as a "rule-of-thumb" value per QALY gained. Five re-ruptures were not included in the cost-effectiveness analysis due to the fact that no one-year outcome data were available. The average cost of the surgical procedure for a re-rupture was 3,333 euros. As this complication requires advanced surgical reconstruction, sick leave is also longer. This thesis also demonstrates that these patients have a poorer patient-reported outcome[182], which would indicate that surgical treatment is even more cost effective. It is likely that it would be beneficial to treat more patients surgically in order to avoid the costs associated with the re-ruptures. The cost-effectiveness acceptability curve demonstrates that it is 57% likely that surgical treatment is cost effective, with 50,000 euros as the threshold for willingness to pay per QALY. This means that there is evidence in favour of surgical treatment compared with non-surgical treatment from a health-economic perspective.

Main result

Surgical treatment is 57% likely to be cost effective if the willingness to pay per QALY is 50,000 euros.

13.3.3. MAPPING

Health economics is a growing field which is attracting considerable attention from many stakeholders. Very little work has been related to Achilles tendon ruptures and health economy. When performing health-economic evaluations and especially cost-effectiveness analyses, preference-based measurements are of great importance. In health economics, the standard way to calculate QALYs is to use the EQ-5D score, but, as this is not routinely used in Achilles tendon research, opening up this field would enable us to develop an algorithm to convert the EQ-5D into the ATRS. This thesis presents a model for predicting the EQ-5D score for the ATRS with a high R^2 which indicates a high goodness of fit, even though the model was only able to demonstrate a correlation in three of the ten ATRS items. The questions with the best fit were the ones on pain and daily activities and they were shown to be of specific interest. To assess the strength of the mapping algorithm, the publication by Brazier et al.[16] is used. In reviewing more than 30 mapping studies for various condition-specific health states, with a total of 119 different mapping models, Brazier et al. concluded that an R^2 of 0.17 was a poorly fitting model and an R^2 of 0.51 was the better model when mapping condition-specific measurements onto generic measurements. This shows that this model has a very high level of fitness compared with other available mapping models. It is worth noting that this mapping model will only be applicable to relatively healthy patients with an EQ-5D of 0.47 or more. This is not a problem for the patients involved in acute Achilles tendon research and it should be expected when the analysis is used on a population with high EQ-5D scores.

Mapping is increasing in popularity, but it is important to note that its validity is yet to be fully addressed. It has been argued that the translation of one score to another does not mean that the same health preference is being measured[149].There are some fundamental concerns relating to mapping of which it is important to be aware. The first is the difference in sensitivity between the different instruments.

Condition-specific instruments are designed to measure small changes specific to the condition in question, in this case, Achilles tendon rupture, as opposed to generic instruments (EQ-5D) that measure general health. The second is the degree of conceptual overlap, which is the loss of information coupled to dimensions in either of the two instruments. The more overlap that is present, the stronger the mapping function and vice versa. Unfortunately, this is a difficult problem to overcome. The obvious problem with this potential poor validity is overestimating/underestimating utility values. No method is perfect and, even though there is some concern about the use of mapping to generate utility values, it is second best to using preference-based measurements in the first place. Most clinical studies use condition-specific instruments and have not been able to include preference-based ones (e.g. not suitable for the relevant condition) and, as interest in performing QALY-based economic evaluations alongside clinical trials is increasing, mapping is an emerging method to make this possible.

In terms of Achilles tendon rupture research, the EQ-5D has not been used historically as an outcome measurement. With the algorithm presented here, this is now possible and gives researchers the opportunity to perform QALY-based economic evaluations using ATRS scores. As seen in this thesis, being able to measure QALY is a cornerstone when performing health-economic evaluations between different health-care interventions. As the treatment of Achilles tendon ruptures is either surgical or non-surgical, it is ideal for this type of evaluation.

Main result

The Achilles tendon total rupture score can be mapped to the European Quality of Life-5 Dimension Questionnaire.

14
LIMITATIONS

14.1. GENERAL METHODOLOGICAL LIMITATIONS

LIMB SYMMETRY INDEX (LSI)

The LSI is a common way of presenting and measuring the function of the Achilles tendon[160]. The LSI has not been studied extensively with regard to Achilles tendon injuries, but it has been studied in relation to anterior cruciate ligament (ACL) ruptures[42, 131]. As the injury is usually unilateral, the healthy side can be used as a control. The reason for presenting this ratio is to make it easier to understand the result of the recovery. In spite of this, it is important to understand that the non-ruptured side will also be affected by the injury. An LSI of > 90% is regarded as full recovery and assurance to the patient that it is possible to return to pre-injury activities in patients with an ACL rupture[55], however this is not studied in in Achilles tendon ruptures. The reduction in strength on the healthy side will inflate the LSI over time and will therefore lead to a distortion of the recovery on the injured side. It is also important to understand that the LSI ratio is based on two independent tests on each leg which have their own unpredictability and this can lead to an over- or underestimation of the true discrepancy.

14.2. STUDY-RELATED LIMITATIONS

14.2.1 STUDY I

One limitation of this study is the limited number of patients. Ultrasound imaging was planned for the entire RCT study, but, due to hospital reorganisation, we were only able to perform the US assessment on the first 45 patients, which makes it difficult to draw any strong conclusions in terms of re-ruptures. Another limitation is that, even though two experienced radiologists performed the US examinations, varied assessments between the investigators are possible, as inter-rater reliability is missing in the present study.

14.2.2. STUDY II

One potential limitation of this study is that the correlation coefficients presented could be categorised as weak, according to general, simplified guidelines[87]. These guidelines are mostly used for agreement between observer ratings for categorical data. As this was not a test-retest setting but an observation of the association between independent variables, it can be argued that the results showing significant associations are not negligible and might be clinically relevant. Another limitation might be that the patients in the different cohorts used slightly different postoperative rehabilitation protocols. However, the rehabilitation protocols were taken into account in the statistical analyses and did not affect the outcome. Although the study was controlled for possible confounding factors, this was a cohort study with its potential bias.

14.2.3. STUDY III

The obvious limitation to this study is the limited cohort size. This makes it difficult to draw any strong conclusions. Re-ruptures are fortunately uncommon, as previously reported, which makes it difficult to include a large number of patients. However, to our knowledge, this is the largest cohort of reported re-ruptures. The strengths of this study are the use of a strict protocol using validated, well-documented outcome measurements and the fact that all the data were collected by the same experienced physiotherapist. The comparison group was also evaluated using identical methods.

14.2.4. STUDY IV

One limitation is that the costs are calculated from a Swedish perspective, which implies that the results may not be directly transferable to other countries and different health-care systems. Another limitation is that we were not able to include the re-ruptures in the health-related quality-of-life follow-up due to the fact that they were excluded from the one-year follow-up in the original study.

14.2.5. STUDY V

One limitation to this study is that the mapping algorithm presented will only be applicable to fairly healthy patients with an EQ-5D of 0.47 as the lowest possible score. This is to be expected, as the analysis was performed on a sample with a high EQ-5D score. It remains to be determined whether the algorithm is applicable to patients with a poorer health state, i.e. by repeating the experiment on a sample with lower EQ-5D scores.

14.2.6. STUDY VI

Including the analysis of "goodness of fit" in this study adds additional strength compared with previous predictor studies of acute Achilles tendon rupture. However, it should be emphasised that the regression models in this study were limited by the overall poor capacity of the models to predict the dependent outcome, since none of the R-square values was higher than 0.02 and the AUC analyses were no better than chance. This implies that there are other important aspects of the treatment that affect the outcomes in these patients. There has been increasing focus on individualised treatment after an acute Achilles tendon rupture in recent years, which requires a deeper understanding of factors contributing to variations in outcome. Potentially, the current outcome measurements are not sensitive enough to provide us with the answers necessary to improve therapy and outcome. For instance, there is a considerable ceiling effect in the ATRS score. A further limitation of the present study is the multiple univariate regression analyses that were performed, which results in a risk of mass significance and questions the small number of significant findings in this study. Unfortunately, no multivariate models could be performed due to the small number of factors that affected outcome. The use of multivariate models would have allowed for a more in-depth analysis, where explicit sub-groups of patients could have been studied. Finally, this study is limited by the fact that the patients were included from previous RCTs, with different surgical methods and rehabilitation protocols, which entail a risk of transfer bias.

15

CONCLUSIONS

Conclusions from this thesis

Study I

Acute ultrasonography can be a helpful tool in selecting treatment in order to reduce re-ruptures and improve outcome.

Study II

Longer duration of operative time leads to the upregulation of healing metabolites.

Study III

Patients with re-ruptures have long-term deficits in terms of functional outcome.

Patients with re-ruptures have a poorer patient-reported outcome than those who have sustained primary ruptures.

Study IV

It is more expensive to treat an Achilles tendon rupture surgically than non-surgically.

When the willingness to pay is 50,000 euros, there is a 57% likelihood of surgical treatment being cost effective.

Study V

It is possible to develop an algorithm to convert the ATRS to the EQ5D in order to use it for health-economic evaluations.

Study VI

Increased age is a negative predictor of outcome one year after an acute Achilles tendon rupture.

16
FUTURE PERSPECTIVES

At the end of 2018, there were more than 10,000 publications on Achilles tendon ruptures in the PubMed database. Even with so many publications and high-quality research, there is still an ongoing debate about whether or not these patients require surgery and the management of these patient varies considerably even within Sweden. Very little is still known about the economic impact of the injury and the factors that have a major effect on outcome and might therefore be clinically useful as predictors of outcome and guide us in treating these patients. Future research necessitates that we continue to focus on individualisation, both initial treatment and rehabilitation. There is also a need to combine traditional high-level studies (RCTs or prospective cohorts) with larger register studies with innovative methodologies.

After reading this thesis, it is clear that we still have a long way to go in terms of finding strong predictors of outcome. In order to find strong predictors of outcome, it is necessary to have a large dataset of patients with different characteristics in order to identify these differences. We also need to focus more research on patient-reported outcome measurements. The Achilles tendon total rupture score is a good instrument, but it is not good at identifying subtle changes in function and there is a considerable ceiling effect that makes it difficult to distinguish between the patients that have a good recovery.

We also need to further address the economic aspect of this injury in an environment where we can do more for our patients, but where the resources are limited. Health economy is a growing field and the decision-makers are putting increasing pressure on clinicians to justify their management not just from a medical perspective but also from an economic one. At this moment in time, only two health-economic analyses have been conducted on this relatively common injury. This work needs to continue and more work needs to be done to truly understand how Achilles tendon ruptures affect individuals and society as whole.

Since there are such a large number of publications, the broad literature can be puzzling. There is still considerable work to do on improving and understanding how, with the help of surgery and rehabilitation, we can prevent re-rupture, elongation and poor functional recovery. Surgery, both open and minimally invasive, gives surgeons the opportunity for the end-to-end apposition of the tendon, leading to fewer re-ruptures, and, as some evidence suggests improved function and less elongation[62, 63, 91], further research needs to be done to give these findings even more strength.

Finally, as we live in an interesting time in history where technology is developing at an incredible pace, it would be of great interest to take Achilles tendon rupture research into this new era of artificial intelligence and robotic surgery. Perhaps with the aid of artificial intelligence, we can finally obtain answers about which patients need which treatment at a low cost.

17

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18

APPENDICES

Lundberglaboratoriet för Ortopedisk Forskning

ATRS

(Achilles tendon Total Rupture Score)

Alla frågor avser hur du upplever eventuella besvär på grund av din skadade hälsena

Markera med ett kryss i den ruta som bäst motsvarar din uppfattning!

1. Är du begränsad av minskad kraft i vaden/hälsenan/foten?

mycket begränsad	0	1	2	3	4	5	6	7	8	9	10	**inte alls begränsad**	Poäng

2. Är du begränsad av att du blir trött i vaden/hälsenan/foten?

mycket begränsad	0	1	2	3	4	5	6	7	8	9	10	**inte alls begränsad**	Poäng

3. Är du begränsad av stelhet i vaden/hälsenan/foten?

mycket begränsad	0	1	2	3	4	5	6	7	8	9	10	**inte alls begränsad**	Poäng

4. Är du begränsad av smärta i vaden/hälsenan/foten?

mycket begränsad	0	1	2	3	4	5	6	7	8	9	10	**inte alls begränsad**	Poäng

5. Är du begränsad i ditt dagliga liv?

mycket begränsad	0	1	2	3	4	5	6	7	8	9	10	**inte alls begränsad**	Poäng

Lundberglaboratoriet för Ortopedisk Forskning

Alla frågor avser hur du upplever eventuella besvär på grund av din skadade hälsena

Markera med ett kryss i den ruta som bäst motsvarar din uppfattning!

6. Är du begränsad när du går på ojämnt underlag?

mycket begränsad	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**inte alls begränsad**	Poäng
	0	1	2	3	4	5	6	7	8	9	10		

7. Är du begränsad när du går raskt uppför en trappa/backe?

mycket begränsad	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**inte alls begränsad**	Poäng
	0	1	2	3	4	5	6	7	8	9	10		

8. Är du begränsad vid aktiviteter som innebär att springa?

mycket begränsad	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**inte alls begränsad**	Poäng
	0	1	2	3	4	5	6	7	8	9	10		

9. Är du begränsad vid aktiviteter som innebär att hoppa?

mycket begränsad	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**inte alls begränsad**	Poäng
	0	1	2	3	4	5	6	7	8	9	10		

10. Är du begränsad att utföra hårt fysiskt arbete?

mycket begränsad	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**inte alls begränsad**	Poäng
	0	1	2	3	4	5	6	7	8	9	10		

Achilles tendon Total Rupture Score (ATRS)

Hospital Number: **Date:**

Date of rupture: **Injured Side:**

Date of repair/reconstruction:

Please rate your current limitations; 0 is no limitation, 10 is severe limitation, circle your answer to the following questions.

1. Are you limited due to decreased strength in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

2. Are you limited due to progressive tiredness in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

3. Are you limited due to stiffness in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

4. Are you limited due to pain in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

5. Are you limited during activities of daily living?

0 1 2 3 4 5 6 7 8 9 10

6. Are you limited when walking on uneven ground?

0 1 2 3 4 5 6 7 8 9 10

7. Are you limited when walking quickly up stairs or up a hill?

0 1 2 3 4 5 6 7 8 9 10

8. Are you limited during activities that include running?

0 1 2 3 4 5 6 7 8 9 10

9. Are you limited during activities that include jumping?

0 1 2 3 4 5 6 7 8 9 10

10. Are you limited in performing heavy physical work?

0 1 2 3 4 5 6 7 8 9 10

PAS SWEDISH

Sandberglaboratoriet för Ortopedisk Forskning

Laboratoriet för muskelfunktion och rörelseanalys

Ringa in det alternativ som bäst överensstämmer med din nivå just nu.

Fysisk aktivitetsnivå JUST NU

Ta hänsyn till vad du arbetar med, samt din fritid, motion och idrott

1 **Knappast någon fysisk aktivitet alls.**

2 **Mest stillasittande, ibland promenad, lättare trädgårdsarbete, eller liknande.**

3 **Lättare fysisk ansträngning omkring 2-4 timmar per vecka, t.ex. promenader, cykling, dans, ordinärt trädgårdsarbete, eller liknande.**

4 **Mer ansträngande motion 1-2 timmar per vecka t.ex. tennis, simning, löpning, motionsgymnastik, cykling (spinning), dans, fotboll, innebandy, tyngre trädgårdsarbete, byggarbete, eller liknande**
***ELLER* lättare fysisk aktivitet (enligt nivå 3) mer än 4 timmar per vecka**

5 **Mer ansträngande motion minst 3 timmar per vecka t.ex. tennis, simning, löpning, motionsgymnastik, cykling (spinning), dans, fotboll, innebandy, tyngre trädgårdsarbete, byggarbete, eller liknande**

6 **Hård träning regelbundet och flera gånger i veckan, där den fysiska ansträngningen är stor**

PAS ENGLISH

1	Hardly any physical activity
2	Mostly sitting, sometimes a walk, easy gardening or similar tasks
3	Light physical exercise around 2-4 hours a week, e.g. walks, fishing, dancing, normal gardening, including walks to and from shops
4	Moderate exercise 1-2 hours a week, e.g. jogging, swimming, gymnastics, heavy gardening, home repairs or easy physical activities more than 4 hours a week
5	Moderate exercise at least 3 hours a week, e.g. tennis, swimming, jogging etc.
6	Hard or very hard exercise regularly and several times a week, where the physical exertion is great, e.g. jogging, skiing

FAOS

Frågeformulär för patienter med fot- och fotledsbesvär

DATUM: ___________________ PERSONNUMMER: ____________________

NAMN: ____

INSTRUKTIONER: Detta formulär innehåller frågor om hur Du ser på din fot / fotled. Informationen ska hjälpa till att följa hur Du mår och fungerar i ditt dagliga liv. Besvara frågorna genom att kryssa för det alternativ Du tycker stämmer bäst in på dig (ett alternativ för varje fråga). Om Du är osäker, kryssa ändå för det alternativ som känns riktigast.

Symptom

Tänk på de **symptom** Du haft från din fot / fotled under den **senaste veckan** när Du besvarar dessa frågor.

S1. Har foten / fotleden varit svullen?

Aldrig	Sällan	Ibland	Ofta	Alltid
☐	☐	☐	☐	☐

S2. Har Du känt att det maler i foten / fotleden eller hör Du klickande eller andra ljud från foten / fotleden?

Aldrig	Sällan	Ibland	Ofta	Alltid
☐	☐	☐	☐	☐

S3. Har foten / fotleden hakat upp sig eller låst sig?

Aldrig	Sällan	Ibland	Ofta	Alltid
☐	☐	☐	☐	☐

S4. Har Du kunnat sträcka vristen / fotleden helt?

Alltid	Ofta	Ibland	Sällan	Aldrig
☐	☐	☐	☐	☐

S5. Har Du kunnat böja vristen / fotleden helt?

Alltid	Ofta	Ibland	Sällan	Aldrig
☐	☐	☐	☐	☐

Stelhet

Följande frågor rör **stelhet**. Stelhet innebär svårighet att komma igång eller ökat motstånd. Markera graden av stelhet Du har upplevt i din fot / fotled den **senaste veckan**.

S6. Hur stel har din fot / fotled varit när Du just har vaknat på morgonen?

Inte alls	Något	Måttligt	Mycket	Extremt
☐	☐	☐	☐	☐

S7. Hur stelt har din fot / fotled varit efter att Du har suttit eller legat och vilat **senare under dagen**?

Inte alls	Något	Måttligt	Mycket	Extremt
☐	☐	☐	☐	☐

Smärta

P1. Hur ofta har Du ont i foten / fotleden?

Aldrig	Varje månad	Varje vecka	Varje dag	Alltid
☐	☐	☐	☐	☐

Vilken grad av smärta har Du känt i din fot / fotled den **senaste veckan** under följande aktiviteter?

P2. Snurra/vrida på belastad fot

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P3. Sträcka vristen / fotleden helt

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P4. Böja vristen / fotleden helt

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P5.Gå på jämnt underlag

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P6. Gå upp eller ner för trappor

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P7. Under natten i sängläge (smärta som stör sömnen)

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P8. Sittande eller liggande

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

P9. Stående

Ingen	Lätt	Måttlig	Svår	Mycket svår
☐	☐	☐	☐	☐

Funktion, dagliga livet

Följande frågor rör Din fysiska förmåga. **Ange graden av svårighet Du upplevt den senaste veckan vid följande aktiviteter på grund av dina fot / fotledsbesvär.**

A1. Gå nerför trappor

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A2. Gå uppför trappor

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A3. Resa dig upp från sittande

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

Ange graden av **svårighet** Du upplevt med varje aktivitet den **senaste veckan**.

A4. Stå stilla

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A5. Böja Dig, t ex för att plocka upp ett föremål från golvet

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A6. Gå på jämnt underlag

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A7. Stiga i/ur bil

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A8. Handla/göra inköp

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A9. Ta på strumpor

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A10. Stiga ur sängen

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A11. Ta av strumpor

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A12. Ligga i sängen (vända dig, hålla foten i samma läge under lång tid)

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A13. Stiga i och ur badkar/dusch

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A14. Sitta

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A15. Sätta dig och resa dig från toalettstol

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A16. Utföra tungt hushållsarbete (snöskottning, golvtvätt, dammsugning etc)

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

A17. Utföra lätt hushållsarbete (matlagning, damning etc)

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

Funktion, fritid och idrott
Följande frågor rör Din fysiska förmåga. **Ange graden av svårighet Du upplevt den senaste veckan vid följande aktiviteter på grund av dina fot / fotledsbesvär.**

SP1. Sitta på huk

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

SP2. Springa

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

SP3. Hoppa

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

SP4. Vrida/snurra på belastad fot / fotled

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

SP5.Ligga på knä

Ingen	Lätt	Måttlig	Stor	Mycket stor
☐	☐	☐	☐	☐

Livskvalité

Q1. Hur ofta gör sig Din fot / fotled påmind?

Aldrig	Varje månad	Varje vecka	Varje dag	Alltid
☐	☐	☐	☐	☐

Q2. Har Du förändrat Ditt sätt att leva för att undvika att påfresta foten / fotleden?

Inte alls	Något	Måttligt	I stor utsträckning	Totalt
☐	☐	☐	☐	☐

Q3. I hur stor utsträckning kan Du lita på Din fot / fotled?

Helt och hållet	I stor utsträckning	Måttligt	Till viss del	Inte alls
☐	☐	☐	☐	☐

Q4. Hur stora problem har Du med foten / fotleden generellt sett?

Inga	Små	Måttliga	Stora	Mycket stora
☐	☐	☐	☐	☐

Tack för att Du tagit dig tid att besvara samtliga frågor!

Frågeformulär och användarguide kan hämtas från: www.koos.nu

Rehabilitation Protocol

Weeks 8-11
Treatment: Shoe with a heel-lift (1.5 cm), crutches as needed for another 1-3 weeks
Exercise program: Visit to physical therapist 2-3 times/wk and home exercises daily
Exercise bike
Ankle range of motion
Sitting heel-rise
Standing heel-rise (2 legs)
Gait training
Balance exercises
Leg press
Leg extension and leg curl
Weeks 11-16
Treatment: Shoe with a heel-lift (1.5 cm) until week 16
Exercise program: Visit to physical therapist 2-3 times/wk and home exercises daily
Exercises as above with increased weight
Standing heel-rise increase to hold at end range of plantar flexion on 1 leg
Step
Walking on mattress
Weeks 16-20
Exercise program: Visit to physical therapist 2-3 times/wk and home exercises
Exercises as above with increase in weights and intensity as tolerated
Slide
Quick rebounding heel-rises
From week 18
Heel-rise in stairs
Side jumps
2-legged jumps
Week 20-24
Exercise program: Visit to physical therapist as needed
Exercises as above with increase in weights and intensity as tolerated
Jog
Side jumps forward
Week 24 and onward
Exercise program: Continued physical therapy if needed
Start group exercise class (similar to aerobics)
Gradual return to sports (dependent on patient ability)

TREATMENT PROTOCOL – ACHILLES TENDON RUPTURE SURGICALLY TREATED

Week 0-2: Visit orthopaedic surgeon
Treatment: Walker brace with 3 heel pads, weight-bearing through the heel as tolerated, use of 2 crutches. Referral to orthopedic technician for shoe heel-lift (use shoe with heel-lift on the healthy side). Wearing the walker brace while sleeping for 6 weeks.
Exercise program: home exercises daily wearing the walker brace

- Isometric submaximal plantar flexion (5x5 sec, once per hour)
- Toe exercises, flexion-extension (3x20 repetitions, once per hour)

After 2 weeks:
Treatment: Walker brace with 2 heel pads (take off the upper pad), full weight-bearing, use of 2 crutches if needed. Allowed to take off the walker brace for washing and aerating the foot. When the walker brace is removed, no weight-bearing or dorsal extension of the foot is allowed.
Exercise program: home exercises daily as described above (increase the intensity)
Visit to physical therapist 2 times per week:

- Exercise bike wearing the walker brace
- Active range of motion (ROM) up to 15° plantar flexion without walker brace (the angle based on the heel-height)
- Active plantar flexion with yellow rubber-band (ROM as above)
- Sitting heel-rise – no weight-bearing (starting position from the heel-height)
- Gait training and balance exercises with the walker brace without crutches.
- Squats (fitness ball behind the back)
- Other knee/hip-exercises with no ankle involvement

After 4 weeks:
Treatment: Walker brace with 1 heel pad (take off the upper pad), full weight-bearing
Exercise program: home exercises daily as described above (increase the intensity)
Visit to physical therapist 2 times per week:

- Exercise bike wearing the walker brace
- Active range of motion (ROM) up to 10° plantar flexion without walker brace
- Active plantar flexion with green rubber-band (ROM as above)
- Sitting heel-rise – with light weight (starting position from the heel-height)
- Supination- and pronation–exercises with rubber-band
- Gait training and balance exercises with the walker brace
- Squats (fitness ball behind the back)
- Other knee/hip-exercises with no ankle involvement

After 5 weeks:
Treatment: Walker brace without heel pad, full weight-bearing
Exercise program: home exercises daily as described above (increase the intensity)
Visit to physical therapist 2 times per week:

- Exercise bike wearing the walker brace
- Active range of motion (ROM) up to 0° plantar flexion without walker brace
- Active plantar flexion in a cable machine (ROM as above)
- Sitting heel-rise – with weight
- Supination- and pronation–exercises in a cable machine
- Gait training and balance exercises with the walker brace
- Squats (fitness ball behind the back)
- Other knee/hip-exercises with no ankle involvement
- Leg press

TREATMENT PROTOCOL – ACHILLES TENDON RUPTURE SURGICALLY TREATED

After 6 weeks: Visit orthopaedic surgeon
Treatment: Wean off walker brace. Use of shoes with heel-lift (bilateral) for 4 weeks, compression stocking to prevent swelling.
Exercise program: ***Important that all exercises are performed slowly and carefully***
Home exercises:

- Active ankle exercises for ROM, ankle exercises (DE, PF, Sup, Pron) with rubber-band, balance exercises, sitting heel-rise, standing heel-rise (50% weight-bearing or less on the injured side), gait training.

Visit to physical therapist 2 times per week:

- Exercise bike
- Active range of motion (ROM)
- Sitting heel-rise – with weight (starting position from the shoe heel-height)
- Standing heel-rise on two legs
- Active plantar flexion in a cable machine (max 0° plantar flexion)
- Heel-rise in leg press (max 0° plantar flexion)
- Supination- and pronation – exercises in a cable machine
- Gait training
- Balance exercises
- Squats
- Step (walk slowly)
- Other knee/hip-exercises with no ankle involvement

After 8 weeks:
Treatment: Use of shoes with heel-lift until 10 weeks after surgery, compression stocking to prevent swelling.
Exercise program: ***Important that all exercises are performed slowly and carefully***
Home exercises: As described above and walking 20 min per day
Visit to physical therapist 2 times per week:

- As described above, increase the intensity
- Sitting heel-rise – with weight (increase the load)
- Standing heel-rise on two legs - transcend gradually to one leg
- Active plantar flexion, supination and pronation in a cable machine
- Heel-rise in leg press
- Cable machine standing leg lifts
- Balance exercises (wobble-board, balance pods - weight bearing in the middle of the foot)

After 12 weeks: Evaluation at Lundberg Lab
Treatment: Use of regular shoes after 10 weeks, barefoot after 12 weeks, compression stocking to prevent swelling.
Exercise program: ***Important to gradually increase the load considering the patient´s status***
Home exercise: Walking 20 min per day
Visit to physical therapist 2 times per week:

- Intensify the exercises by increasing load (as before)
- Increase the load gradually from two leg standing heel-rises to one leg standing heel-rises both concentrically and eccentrically
- Quick rebounding heel-rises (start with two legs)
- Start with gentle jog (thick mattress, in 8´s, zig-zag)
- Start with two-legged jumps and increase gradually

After 14 weeks: Evaluation at Lundberg Lab 6 and 12 months after surgery, visit orthopaedic surgeon 6 months

- Running outdoors, if the patient has a good technique
- Group training (similar to aerobics, adapted for knee-injured patients)
- Return to sports earliest after 16 weeks (non-contact sports) and 20 weeks (contact sports)
- Possibility for the patient to be evaluated at Lundberg Lab before 6 months if needed to estimate the ability to return to sports.

TREATMENT PROTOCOL –
ACHILLES TENDON RUPTURE NON-SURGICALLY TREATED

Week 0:

Treatment: Walker brace with 3 heel pads, weight-bearing through the heel as tolerated, use of 2 crutches. Referral to orthopedic technician for shoe heel-lift (use shoe with heel-lift on the healthy side).

Walker brace: Allowed to take off the walker brace for washing and aerating the foot. When the walker brace is removed, no weight-bearing or dorsal extension of the foot is allowed. Wearing the walker brace while sleeping.

Exercise program: home exercises daily wearing the walker brace – move the toes several times a day

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After 2 weeks:

Treatment: Walker brace with 2 heel pads (take off the upper pad), full weight-bearing, use of 2 crutches if needed.

Exercise program: home exercises as described above.

After 4 weeks:
Treatment: Walker brace with 1 heel pad, full weight-bearing

Exercise program: home exercises daily as described above

After 6 weeks:
Treatment: Walker brace without heel pad, full weight-bearing

Exercise program: home exercises daily as described above

After 8 weeks: Visit orthopaedic surgeon

Treatment: Wean off walker brace. Use of shoes with heel-lift (until 14 weeks after injury), compression stocking to prevent swelling.

Exercise program: ***Important that all exercises are performed slowly and carefully***

Home exercises:
- Active ankle exercises for ROM, ankle exercises (DE, PF, Sup, Pron) with rubber-band, balance exercises, sitting heel-rise, standing heel-rise (50% weight-bearing or less on the injured side), gait training.

Visit to physical therapist 2 times per week:
- Exercise bike
- Active range of motion (ROM)
- Sitting heel-rise – with weight (starting position from the shoe heel-height)
- Standing heel-rise on two legs
- Active plantar flexion with a rubber-band (max 0° plantar flexion)
- Supination- and pronation – exercises with a rubber-band
- Gait training
- Balance exercises (not wobble boards or balance pods)
- Squats (fitness ball behind the back)
- Other knee/hip-exercises with no ankle involvement

TREATMENT PROTOCOL –
ACHILLES TENDON RUPTURE NON-SURGICALLY TREATED

After 10 weeks:

Treatment: Use of shoes with heel-lift until 14 weeks after injury, compression stocking to prevent swelling.
Exercise program: ***Important that all exercises are performed slowly and carefully***
Home exercises: As described above
Visit to physical therapist 2 times per week:

- As described above, increase the intensity
- Sitting heel-rise – with weight (starting position from the shoe heel-height)
- Standing heel-rise on two legs - transcend gradually to one leg
- Active plantar flexion, supination and pronation in a cable machine
- Heel-rise in leg press
- Balance exercises (wobble-board, balance pods-weight bearing in the middle of the foot)
- Step (walk slowly)
- Cable machine standing leg lifts

After 12 weeks: Evaluation at Lundberg Lab

Treatment: Use of shoes with heel-lift until 14 weeks after injury, compression stocking to prevent swelling.

Exercise program: ***Important that all exercises are performed slowly and carefully***

Home exercises: As described above and walking 20 min per day

Visit to physical therapist 2 times per week:

- As described above, increase the intensity

After 16 weeks:
Treatment: Use of regular shoes after 14 weeks, barefoot after 16 weeks, compression stocking to prevent swelling.

Exercise program: ***Important to gradually increase the load considering the patient´s status***

Home exercise: Walking 20 min per day

Visit to physical therapist 2 times per week:

- Intensify the exercises by increasing load (as before)
- Increase the load gradually from two leg standing heel-rises to one leg standing heel-rises both concentrically and eccentrically
- Start with gentle jog (thick mattress, in 8´s, zig-zag)
- Start with two-legged jumps and increase gradually

After 18 weeks: Evaluation at Lundberg Lab 6 and 12 months after injury, visit orthopaedic surgeon 6 months.

- Running outdoors, if the patient has a good technique
- Group training (similar to aerobics, adapted for knee-injured patients)
- Return to sports earliest after 20 weeks (non-contact sports) and 24 weeks (contact sports)
- Possibility for the patient to be evaluated at Lundberg Lab before 6 months if needed to estimate the ability to return to sports.

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ☐

I have slight problems in walking about ☐

I have moderate problems in walking about ☐

I have severe problems in walking about ☐

I am unable to walk about ☐

SELF-CARE

I have no problems washing or dressing myself ☐

I have slight problems washing or dressing myself ☐

I have moderate problems washing or dressing myself ☐

I have severe problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ☐

I have slight problems doing my usual activities ☐

I have moderate problems doing my usual activities ☐

I have severe problems doing my usual activities ☐

I am unable to do my usual activities ☐

PAIN / DISCOMFORT

I have no pain or discomfort ☐

I have slight pain or discomfort ☐

I have moderate pain or discomfort ☐

I have severe pain or discomfort ☐

I have extreme pain or discomfort ☐

ANXIETY / DEPRESSION

I am not anxious or depressed ☐

I am slightly anxious or depressed ☐

I am moderately anxious or depressed ☐

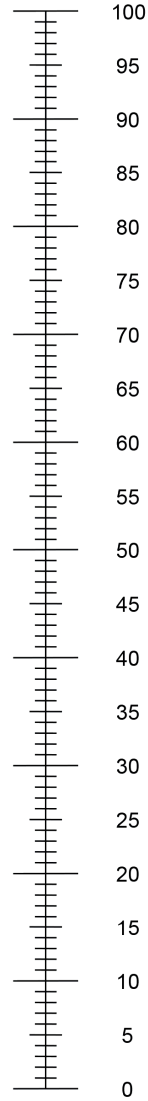
I am severely anxious or depressed ☐

I am extremely anxious or depressed ☐

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = $\boxed{}$

The best health
you can imagine



The worst health
you can imagine

19

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