FACULTY OF HEALTH AND MEDICAL SCIENCES
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PhD thesis

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Acute Achilles Tendon Rupture

Assessment of non-operative treatment

CORH

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Preface and acknowledgements

Some years back I got an advice from a good friend and colleague: '… just get in his slipstream and hold on!' I did, and for three good years I have had the pleasure of taking part in an idea, greater than this thesis, turning into reality; the creation of the research unit Clinical Orthopedic Research Hvidovre - CORH. This PhD thesis is based on clinical studies carried out from 2010 to 2013, in the shaping of CORH. The work was funded by the Copenhagen University Hospital Hvidovre.

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Abbreviations

ASA	American Society of Anesthesiologists
ATRS	Achilles tendon Total Rupture Score
ICC	Intraclass correlation Coefficient
MDC	Minimal Detectable Change
MRI	Magnetic Resonance Imaging
PROM	Patient Reported Outcome Measure
RCT	Randomized Controlled Trial
RSA	Roentgen Stereophotogrammetric Analysis
SEM	Standard Error of the Measurement
US	Ultrasound

English summary

Background: Acute Achilles tendon rupture is a frequent and potentially disabling injury. Over the past decade a change in treatment of acute Achilles tendon rupture away from operative towards non-operative treatment has taken place. However, the optimal non-operative treatment protocol remains to be clarified, particularly the role of weight-bearing during early rehabilitation. Also, there is a need for a clinically applicable and accurate measurement to detect patients in risk of developing Achilles tendon elongation.

Purpose: The aim of this PhD thesis was to evaluate non-operative treatment of acute Achilles tendon rupture.

Methods: In *study I*, a cross sectional survey was performed investigating the chosen treatment protocols across Scandinavia. In *study II*, the effect of immediate weight-bearing on patient reported and functional outcomes was investigated in a randomized controlled trial (RCT). In *study III*, the effect of immediate weight-bearing on the biomechanical properties of the plantar flexor muscle-tendon complex was investigated in an RCT. In *study IV*, validity, reliability and agreement of a novel ultrasound measurement of Achilles tendon length and elongation was tested.

Results: *Study I* found surgery to be the preferred treatment in 83% of departments in Denmark, 92% in Norway, 65% in Sweden, and 30% in Finland ($p < 0.001$). *Study II and III* showed no statistically significant effects of controlled early weight-bearing at one year follow up except from a better health-related quality of life in the weight-bearing group ($p=0.009$). Compared to the unaffected limb, the affected limb had decreased stiffness (77%, $p<0.001$) and strength (93%, $p=0.009$) of the plantar flexor muscle-tendon complex. *Study IV* showed excellent intra-rater reliability (ICC 0.96, SEM 3.7mm and MDC 10.3mm), inter-rater reliability (ICC 0.97, SEM 3.3mm and MDC 9.3mm) and validity (measurement error 2%).

Conclusion: Treatment algorithms across Scandinavia showed considerable variation, though operative treatment and controlled early weight-bearing was the preferred treatment in Denmark, Norway and Sweden. Immediate weight-bearing was found to be safe and recommendable in non-operative treatment of acute Achilles tendon rupture. The novel ultrasound measurement showed excellent reliability and acceptable validity and agreement.

Danish summary

Baggrund: Akut akillesseneruptur er en hyppig og potentielt invaliderende skade. Behandlingen har gennem det sidste årti bevæget sig væk fra operation i retning af ikke-operativ behandling, men den bedste ikke-operative behandlingsprotokol mangler fortsat at blive afklaret, især hvilken rolle tidlig vægtbæring har i rehabiliteringen. Endvidere er der behov for et klinisk relevant og præcist mål til at identificere de patienter som er i risiko for at udvikle akillesseneforlængelse.

Formål: Formålet med denne ph.d.-afhandling var at evaluere ikke-operativ behandling af akut akillesseneruptur.

Metode: S*tudie I* var et spørgeskemabasseret tværsnitsstudie undersøgende de valgte behandlings protokoller i Skandinavien. *Studie II* var et randomiseret kontrolleret studie undersøgende effekten af vægtbæring på patient rapporterede og funktionelle effektmål. *Studie III* var et randomiseret kontrolleret studie undersøgende effekten af vægtbæring på de biomekaniske egenskaber af plantar-flexor-muskelsene-komplekset. I *studie IV* blev validitet og pålidelighed af et nyt ultralyds mål til bestemmelse af akillessenelængde testet.

Resultater: *Studie I* viste at operation er den foretrukne behandling i 83% af afdelinger i Danmark, 92% i Norge, 65% i Sverige og 30% i Finland (p <0,001). *Studie II og III* viste ingen statistisk signifikant effekt af kontrolleret tidlig vægtbæring ved et års follow-up, fraset en bedre helbredsrelateret livskvalitet i den vægtbærende gruppe (p = 0,009). Sammenlignet med det ikke-afficerede ben, havde det afficerede ben reduceret stivhed (77 %, p <0,001) og styrke (93 %, p = 0,009) af plantar-flexor-muskelsene-komplekset. *Studie IV* viste god intra-rater pålidelighed (ICC 0,96, SEM 3.7mm og MDC 10.3mm), inter-rater pålidelighed (ICC 0,97, SEM 3.3mm og MDC 9.3mm) og validitet (målefejl 2%).

Konklusion: Behandlingsprotokoller i Skandinavien viste stor variation. Operativ behandling med kontrolleret tidlig vægtbæring var den mest anvendte behandling på danske, norske og svenske sygehuse. Vægtbæring blev fundet at være sikkert og anbefalelsesværdigt ved ikke-operativ behandling af akut akillesseneruptur. Det nye ultralydsmål viste god pålidelighed og validitet.

1 Introduction

'This tendon, if bruised or cut, causes the most acute fevers, induces choking, deranges the mind, and at length brings death'

Hippocrates

The Achilles tendon was named after the Greek hero Achilles, the central character and greatest warrior of Homer's Iliad. To protect Achilles from harm, his mother dipped him into the River Styx. However, his heel was left vulnerable, as it was not covered by water. During the Trojan War, Achilles was struck on his unprotected heel by a poisoned arrow and died[43].

The Achilles tendon is also called the calcaneal tendon. The oldest known written record using the term 'Achilles tendon' is found in the work Corporis Humani Anatomia, published in 1693 by the Dutch anatomist Philip Verheyen (figure 1)[29].

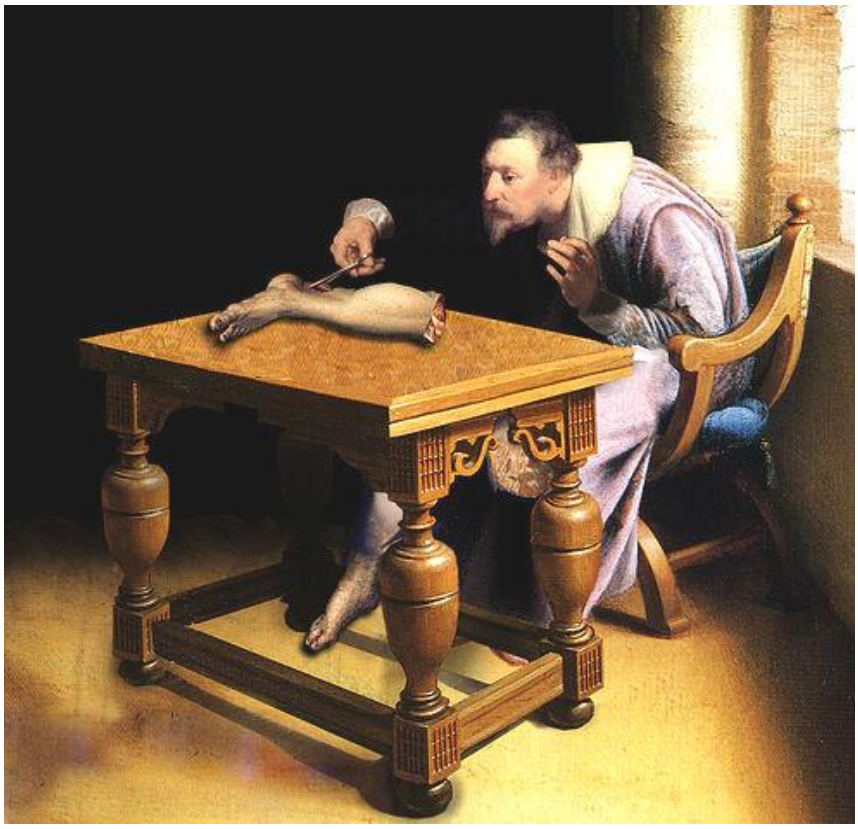

Figure 1

As a young man Philippe Verheyen had his lower limb amputated due to illness. It was preserved to be buried with him. In his older days he investigated his own limb to see if his phantom pain in fact originated from the actual amputated limb.

Title: Philippe Verheyen Dissecting His Amputated Limb (1715-1730), Artist unknown.

Source: Collection of Pieter Deheijde.

Acute Achilles tendon rupture is, and has always been, a problem for the affected person and for society. It affects people in their most active years and follows them for the rest of their life. The area has been the focus of intense research over the past decades and treatment protocols have been continuously debated.

Over the past five to ten years a shift towards non-operative treatment has been observed[8,74], notoriously raising the question: 'What is the optimal non-operative treatment protocol for acute Achilles tendon rupture?' It is my hope that this thesis will aid in illuminating this question.

2 The Achilles tendon

"If you can't explain it simply, you don't understand it well enough"

Albert Einstein

2.1 Anatomy

The Achilles tendon is the strongest and thickest tendon in the body. It transfers energy from the leg to the foot and is essential for walking, running and postural control. It serves to transmit force from the suralis muscle to the calcaneal bone.

2.1.1 The suralis muscle

As the name indicates, the suralis muscle consist of three parts: the gastrocnemius muscle containing two superficial heads and the soleus muscle containing the profound head (figure 2 and 3). The gastrocnemius muscle is two headed originating from the medial and lateral femur epicondyles, respectively, making the suralis muscle span two joints: the knee and ankle joint.

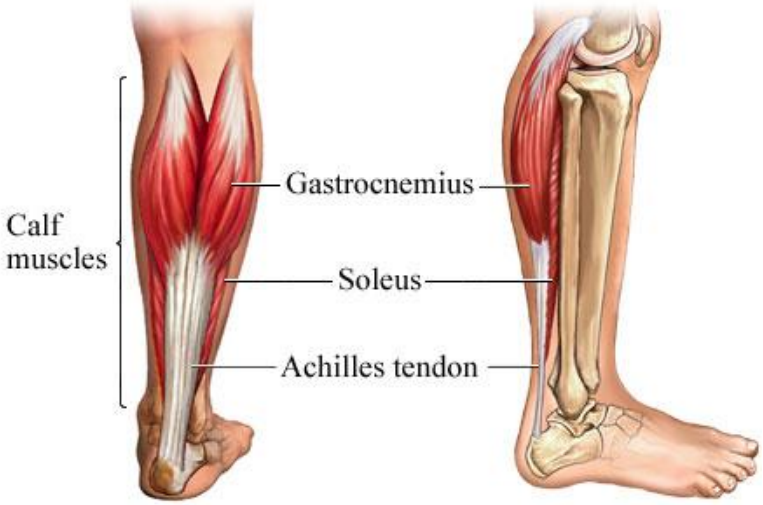

***Figure 2**: The anatomy of the Achilles tendon and the suralis muscle.*

The muscle fibers are mainly type II and 6-8cm long, making them capable of explosive contractions used for jumping and running. They insert in a profound, gathered tendon sheet. The medial head is the most distal. The soleus muscle originates from the posterior site of tibia. The muscle fibers are 2-3 cm long and organized in a multipennat pattern. The soleus muscle consist mainly of type I fibers making it the workhorse in postural control and walking. The soleus muscle inserts in a superficial tendon sheet that gathers with the tendon sheet of the gastrocnemius muscle half way down the calf to form the Achilles tendon (figure 2 and 3). [1,16,137]

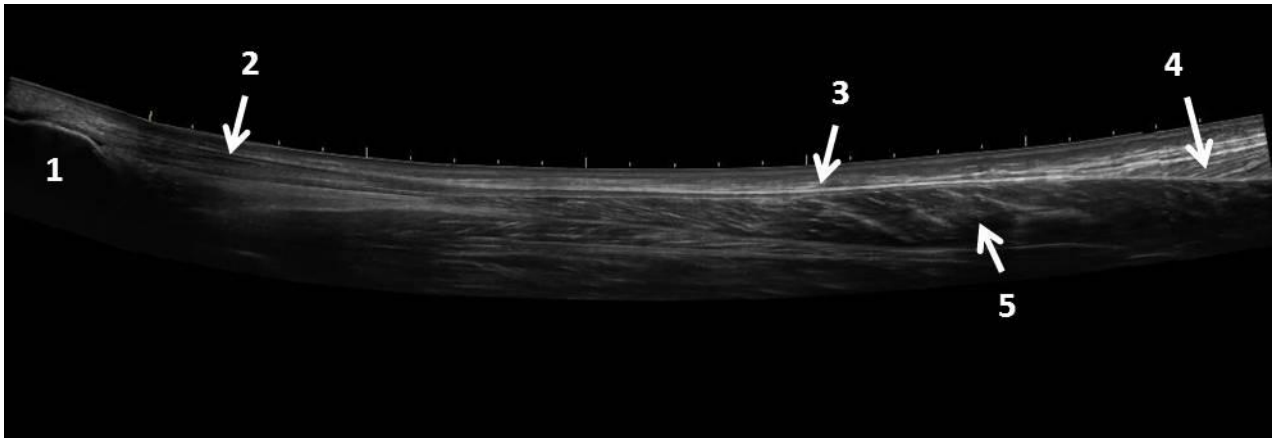

***Figure 3**: A panoramic ultrasound picture of the calf: 1) Calcaneus, 2) The Achilles tendon, 3) the convergence of the tendon sheets of the suralis and soleus muscles, 4) the gastrocnemius muscle, and 5) the soleus muscle.*

2.1.2 The Achilles tendon

The Achilles tendon has a cross sectional area of approximately ½ cm^2 (figure 2 and 3). It rotates 180° in supination before inserting at the calcaneal bone[16]. This spiraling of the tendon contributes to the elastic recoil of the tendon[93]. The insertion in the calcaneal bone, the enthesis, has been estimated to be four times as strong as the mid substance of the tendon[75]. The Achilles tendon is covered by a tendon sheet on the posterior/superior side of the tendon, but not at the anterior/inferior side. The plantaris tendon is found within the tendon sheet just medial to the Achilles tendon.

2.1.3 Architecture of the tendon

The Achilles tendon is built of collagen molecules in a complex matrix of left and right turned helices bound together by proteoglycans[16]. Type I collagen constitutes 95% of the total collagen. The remaining 5% consist of type III and V, mainly located to the enthesis and the epitenon. The tendon is a hierarchical structure composed of collagen molecules, fibrils, fiber bundles, fascicles and tendon units that run parallel to the tendon's axis (figure 4)[116]. Fibers and fascicles are enclosed by the epitenon, which is a fine, loose connective-tissue sheath containing the vascular, lymphatic, and nerve supply to the tendon[137]. The dominant cell type is the fibroblast (tenoblasts and tenocytes), which align in rows between collagen fiber bundles and produce the collagen matrix.

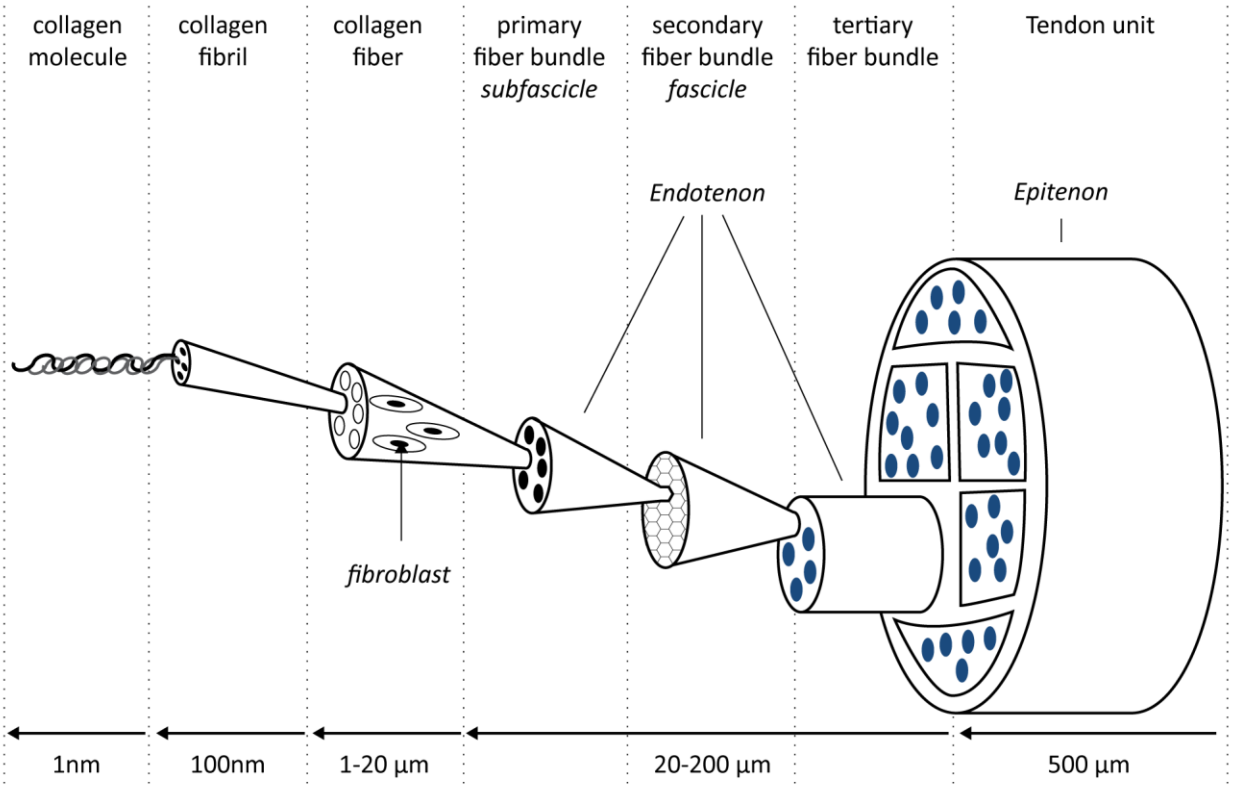

***Figure 4**: A schematic drawing of the tendon as a multi-unit hierarchical structure (modified from Wang et al., 2006)*

2.1.4 The plantar flexor muscle-tendon complex

While the suralis muscle is by far the strongest plantar flexing muscle, also the plantaris muscle, the flexor hallucis longus, the flexor digitorum longus and the tibialis posterior muscle contribute to plantar flexion as they run behind the rotational axis of the ankle joint[16]. Due to this, some people are able to plantar flex the ankle after a total Achilles tendon rupture. Together, these five muscles and their respective tendons constitute the plantar flexor muscle-tendon complex.

2.1.5 Circulation

Vascularization of the Achilles tendon can be divided into three areas: the upper third, the middle third and the lower third; correspondent to the areas from where the tendon receives its blood supply: the musculotendinous junction, the paratenon and the osseotendinous junction[1,128]. The upper and lower third are mainly supplied by the posterior tibial artery[1], whereas the middle third is supplied by the peroneal artery[128]. It has been argued that the mid portion of the Achilles tendon is especially susceptible to rupture due to its poor blood supply[1], however, newer studies using micro dialysis have shown blood supply in the Achilles tendon to increase proportionally with muscle tissue[137].

2.1.6 Innervation

Innervation of the Achilles tendon is found in the epitenon. The sensory branches originate from the contributing muscles and from the nearby cutaneous nerves[93]. The suralis and the saphenous nerves run lateral and medial to the Achilles tendon leaving them exposed to injury during surgery on the Achilles tendon. The suralis muscle is innervated from the tibial nerve.

2.2 Biomechanical properties

The Achilles tendon is remarkably strong and can withstand stresses that by far exceed those transmitted during daily activities and sports. It has been estimated that the peak force transmitted through the Achilles tendon during running is 9 kN, which is equivalent to 12.5 times the body weight[59].

Our knowledge on biomechanical properties of tendons is mainly derived from animal models and cadaveric studies[16]. A typical tendon stress-strain curve is seen in figure 5.

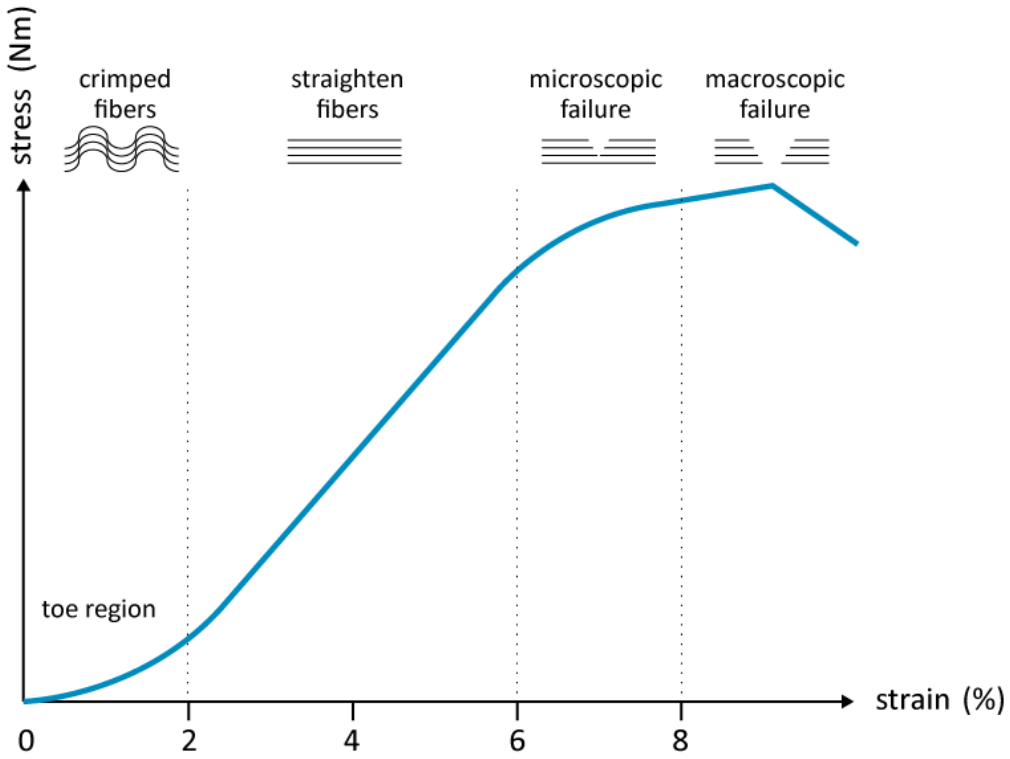

***Figure 5**: A schematic drawing of the stress-strain curve for the Achilles tendon (modified from Wang et al., 2006)*

The first 2% of elongation represents the stretching-out of the collagen fibers[137]. As all fibers become stretched the stress-strain curve becomes linear until the tendon starts failing and microscopic tearing occurs. Beyond a 8–10% strain, macroscopic failure occurs. The slope of the curve represents the tendon stiffness and is referred to as Young's modulus. Stiffness has been shown to be associated with the tendons efficiency in storing and releasing energy[135]. The area under the loading stress-strain curve represents the tendons ability to store energy.

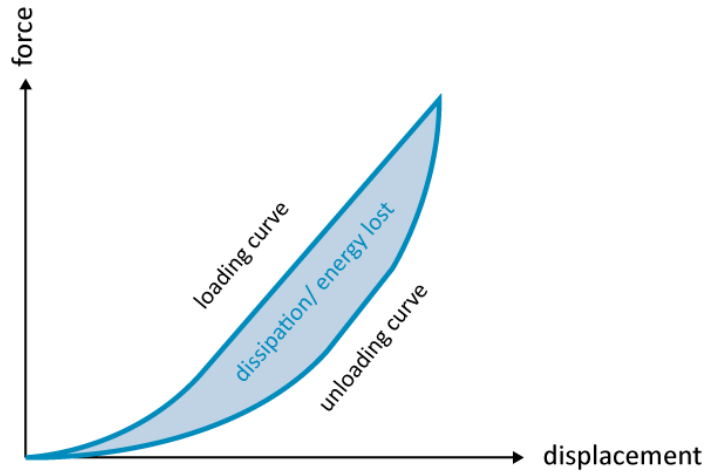

***Figure 6**: A schematic drawing of energy absorption in a tendon and energy lost during the coil-recoil process.*

The area under the un-loading curve represents the tendons ability to release energy. The area between the two curves represents the energy lost in the coil-recoil process (figure 6). This ability to store and release energy is extremely important for the stretch-shortening cycle[22], as it has been demonstrated that up to 60% of the work involved in repetitive jumping exercises is generated in the Achilles tendon[135]. If the tendon is held maximally stretched, the tension will decline over time, a phenomenon referred to as torque relaxation (figure7)[18].

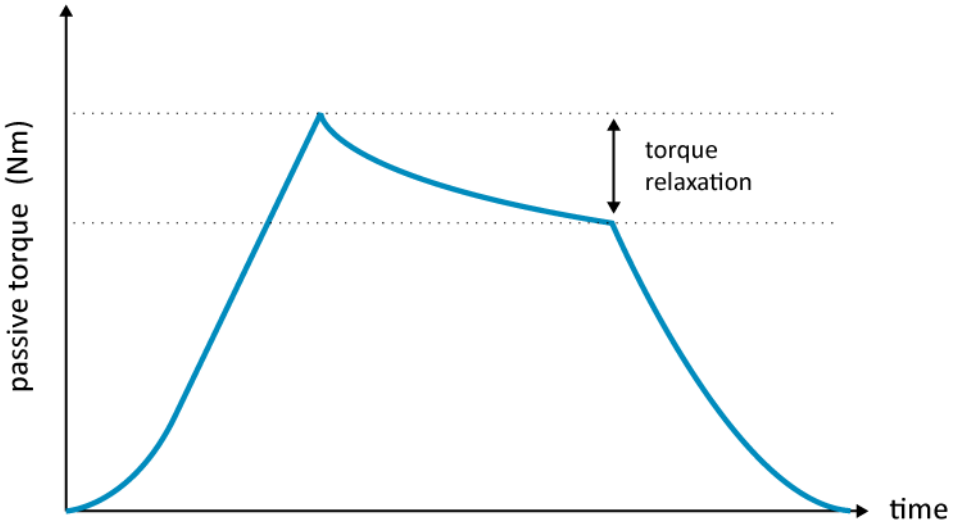

***Figure 7**: A schematic drawing of the phenomenon torque relaxaion.*

2.3 Healing after rupture

Tissue turnover in the Achilles tendon is an extremely slow process. It has been shown that the core of the Achilles tendon is formed before the age of 20 and essentially not renewed thereafter[40]. In contrast, the periphery of the tendon is able to respond to mechanical forces by altering its structure, composition, and mechanical properties. An adaptation mediated by the fibroblasts through biochemical signaling[137].

Tendon repair can be described in three overlapping phases: 1) the inflammatory phase, 2) the proliferative phase, and 3) the remodeling phase (figure 8). In the inflammatory phase, the bleeding caused by the rupture leads to hematoma and activation of platelets and neutrophils, which again leads to the release of growth factors, chemotactic factors and vasoactive factors. The vascular permeability is increased, inflammatory cells are recruited and a tendon granuloma is

produced[6,32]. In the proliferative phase, angiogenesis allows for vascular and neuronal ingrowth in the granuloma. The fibroblasts produce collagen (mainly type 3) and the mechanical strength of the granuloma gradually increases. After 10 to 14 days a tendon callus has been produced gluing the torn tendon ends together. Production of collagen type 1 gradually takes over and the callus reaches its largest size. The large transverse area of the tendon compensates for its weak composition. In the remodeling phase, the randomly deposited collagen fibers are resorbed and replaced to produce better architecture and cross-linking. The remodeling phase starts one to three months after rupture and lasts for several years[6,32,66,112].

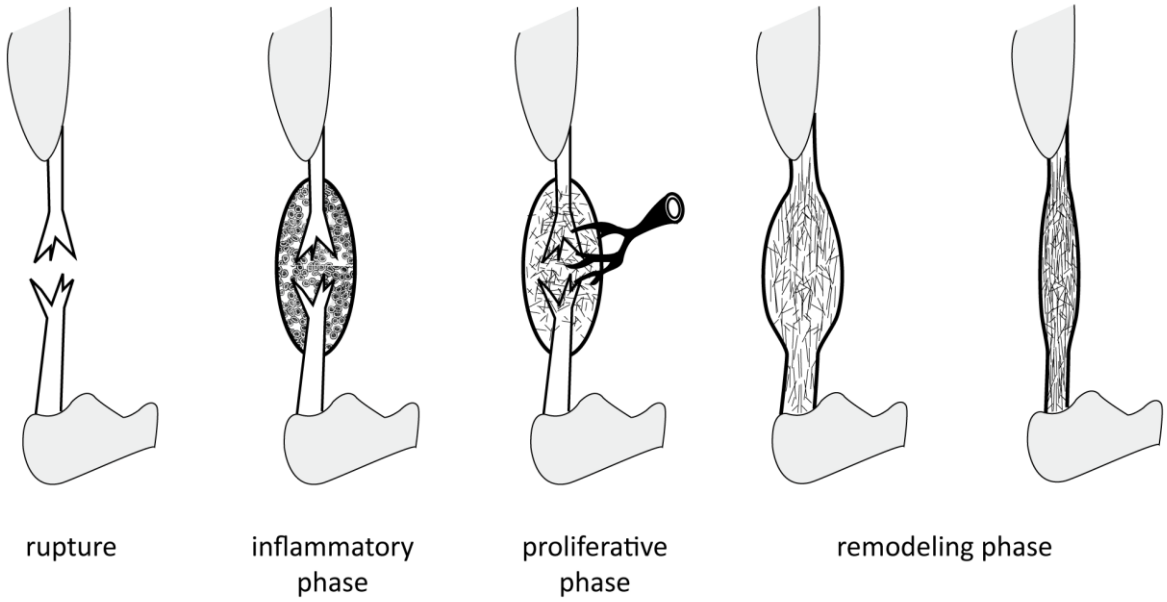

***Figure 8**: A schematic drawing of the three healing phases of an Achilles tendon (modified from Aspenberg et al., 2007)*

2.3.1 Stimulation by mechanical loading

It is well described that mechanical loading improves tendon repair [6,34,119,66,73]. Clinical studies looking at flexor tendons have found controlled early motion to increase strength and avoid adhesions after surgical repair[34,119]. Animal studies have shown a three times increased strength of Achilles tendons rehabilitated with controlled early motion compared to the immobilized ones[73]. Elliason et al. have shown that growth factors in the tendon callus are influenced by loading of the tendon[32,30]. They found more than 150 genes up regulated or down regulated three hours after one loading episode, and conclude that as little as five minutes of loading each day can improve

the strength of the healing tissue[31]. Thus, it seems reasonable to believe that early loading of the tendon under controlled conditions will affect tendon healing beneficially.

2.3.2 Stimulation by growth factors

This leads to the question whether mechanical loading can be replaced by drugs. Several growth factors have been shown to stimulate tendon repair in animal models[6]; among those platelet-derived growth factors[10,42], fibroblast growth factors[25], vascular endothelial growth factors[145] and insulin-like growth factors[63]. For those to be applied in the treatment of acute Achilles tendon rupture several questions need to be answered concerning time and dose of application and safety issues. In an attempt to shortcut those considerations some clinicians have started treatment with platelet concentrate derived from the patient's own blood, as platelets contain a number of growth factors[134]. Animal studies have shown promising results[134], but the present clinical studies have not shown any effect of platelet derivates[106].

2.6 Etiology of rupture

There is little agreement on the etiology of acute Achilles tendon rupture. Several theories have been suggested[86]:

1) Tendon degeneration has been suggested to predispose rupture as histological studies have shown degenerative changes in specimens obtained from rupture sides[5,68]
2) The collagen fibrils have been found to decrease with age, and therefore age has been suggested as a predisposing factor[120]
3) Cortocosteroids injected into rabbit tendons caused necrosis and delayed healing[7]. Furthermore, the anti-inflammatory response of corticosteroid might mask the symptoms of micro-lesions and make people continue high activity even though the tendon is damaged[12]. However, prospective and retrospective studies have not been able to show causality between the use of corticosteroid and acute Achilles tendon rupture[70,36]
4) Fluoroquinolones have been associated with acute Achilles tendon rupture. Intracellular changes and a decrease in fibril diameter have been found in rats treated with fluoroquinolones[109,110,111], and a large cohort study looking at 6.4 million people found the use

of quinolones to be strongly associated with an increased risk of Achilles tendon rupture (odds ratio 2.0)[143]

5) Avascularity and heat necrosis have also been suggested as possible predisposing factors[1,142]
6) Finally Barfred demonstrated that healthy tendons ruptured when maximal stress was applied in combination with supination of the calcaneus and oblique loading of the tendon[9]

2.7 Epidemiology of rupture

Acute Achilles tendon rupture is a frequent injury that typically occurs among young active adults. The incidence is 11 to 37 per 100,000 person-years and the male:female ratio is 5:1[45,65,74,82]. A bimodal age distribution has been proposed with a maximum incidence of sports injuries in the fourth decade of life followed by a second, but lower, peak of other injuries in the eighth decade[82]. The latest Danish incidence study published in 1998 showed an increase in incidence from 18 per 100.000 person-years in 1984 to 37 per 100.000 person-years in 1996. 74% of the ruptures were sports-related and 89% of those occurred in racket and ball games[45].

2.8 Diagnosis of rupture

Patients with acute Achilles tendon rupture typically present with a history of sudden pain in the Achilles tendon accompanied by a loud snapping sound. The patient often feels he/she was kicked or hit by something, though the spectators can tell it was not the case. The rupture often occurs in push off with extended knee. The clinical examination reveals a palpable gap at the site of the rupture, typically 4-5cm above calcaneus. The ability to push off during walking and to plantar flex against resistance is weak or absent[69,85,93].

A number of clinical tests have been described, of which Thompsons test (the calf squeeze test) and Matles test have the best sensitivity (0.96 and 0.88 respectively) and specificity (0.93 and 0.85 respectively)[69]. Thomsons test is performed with the patient lying prone and the feet hanging freely, while the calf is squeezed from side to side and plantar flexion of the foot is observed. The test is positive if plantar flexion is absent[130]. Mattles test is performed with the patient lying prone, the knees are bent 90 degrees and the position of the ankles and feet is observed during flexion of the knee. The test is positive if the foot on the affected side falls into neutral or into dorsiflexion[72].

Ultrasound (US) and Magnetic Resonance Imaging (MRI) are used as diagnostic tools in some regions[20]. However, the high sensitivity and specificity of Thompsons and Mattles tests taken into consideration, one should be careful not to be misled by the imaging modalities. US and MRI examinations are not recommended for routine use[26]. The diagnosis of acute Achilles tendon rupture is primarily clinical[69].

3 Treatment of acute Achilles tendon rupture

The whole problem with the world is that fools and fanatics
are always so certain of themselves but wiser people so full of doubts
Bertrand Russel

The first description of acute Achilles tendon rupture was done by Ambroise Paré (1510-1590). He described the treatment and prognosis as follows: "...This mischance may be amended by long lying and resting in bed and repelling medicines applied to the part....neither must we promise to ourselves or to the patient certain or absolute health. But on the contrary at the beginning of the disease we must foretell that it will never be so cured, and that some relics may remain..."[58]. In 1736 Jean Louis Petit started treating patients in equinus position. The patient was treated prone with the knees flexed and the feet plantar flexed. A slipper on the foot was attached to the thigh with pins to maintain plantar flexion. The bandages were removed and reapplied after eight and 15 days. Healing was advanced at 22 days and weight-bearing commenced ten days later[58].

The first published series describing acute Achilles tendon rupture was published by Qenu and Stoianovitch in 1929[100]. They compared the results of 29 non-operatively treated and 39 operatively treated patients, thereby starting an ongoing discussion of whether to treat operatively or non-operatively. During the past fifty years an increased awareness of acute Achilles tendon rupture and treatment modalities developed, and a range of different treatment protocols have been described[57]. The historical diversity of published results and recommendations has led to considerable variation in treatment protocols between departments treating this injury[8].

Treatment of acute Achilles tendon rupture can be divided into two main categories: Operative and non-operative treatment (figure 9). Rehabilitation can be immobilizing or mobilizing. In this thesis, treatment protocols allowing mobilization before the end of the fourth week are categorized as mobilizing. Mobilization can be divided into controlled early motion and early weight-bearing. Some confusion exist concerning terminology as the term dynamic rehabilitation

by some authors refers to the overall term 'mobilization' and by others to 'controlled early motion'. In paper I-III dynamic rehabilitation refers to controlled early motion.

Over the past decade a change in treatment of acute Achilles tendon rupture from operative and immobilizing treatment towards non-operative treatment using controlled early motion has taken place[74].

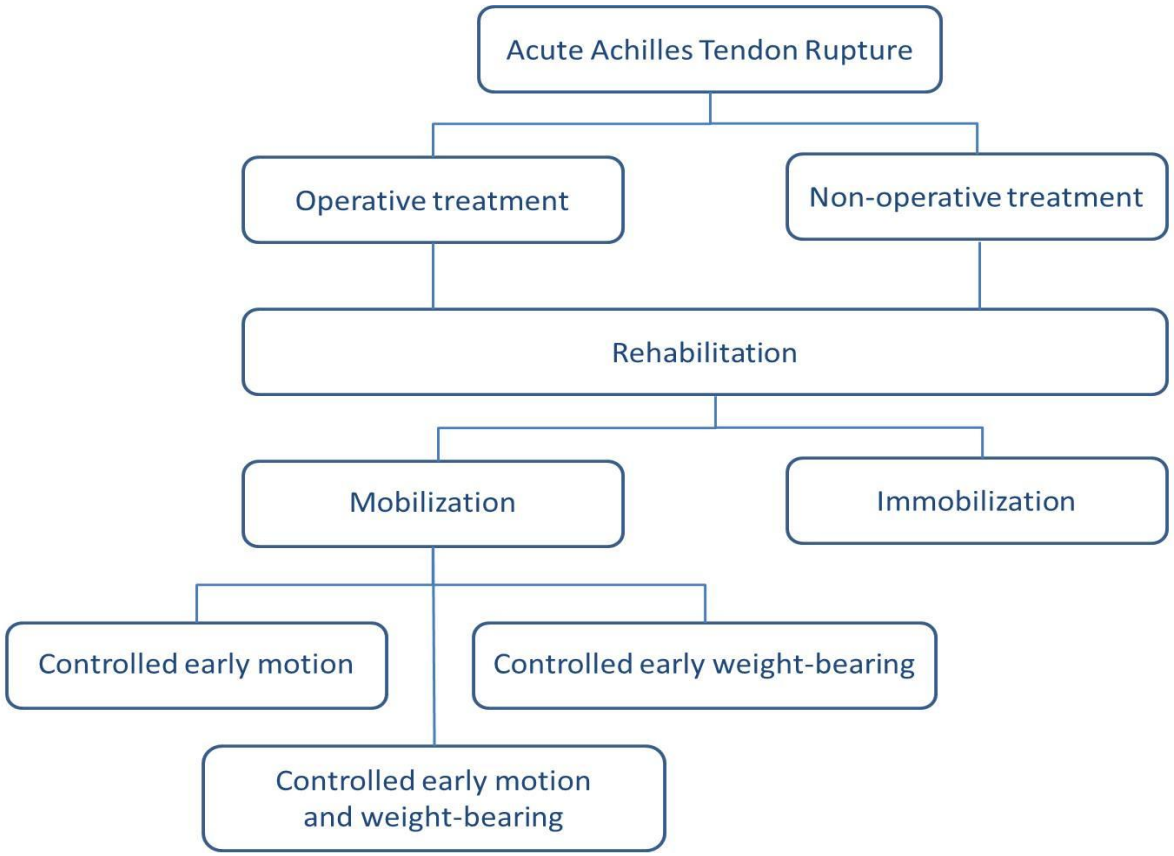

***Figure 9**: A flow diagram to visualize the different treatment and rehabilitation protocols after acute Achilles tendon rupture.*

3.1 Operative vs. non-operative treatment

The first known open repair of an acute Achilles tendon rupture was performed in 1888 by Polaillon[58]. Since then a variety of open, minimally invasive, and percutaneous surgical techniques have been developed and described[3]. Surgical techniques are, however, not addressed in this thesis.

Since the early 80ies, 12 randomized controlled trials (RCT's) and 7 meta-analyses comparing operative and non-operative treatment have been published (table 1).

	No	Mobi-liza-tion	RR-rate (*)	Rec. Opera-tion	Bhan-dari 2002[13]	Khan 2005[56]	Coch-rane 2010[57]	Jiang 2012[48]	Jones 2012[49]	Wilkins 2012[139]	Soro-ceanu 2012[117]
Nistor 1981[89]	105	No	2/5	No	X	X	X	X	X	X	X
Cetti 1993[23]	111	No	3/7	Yes	X	X	X	X	X	X	X
Therman n 1995[129]	50	Yes	?	Maybe	X						X
Schroede r 1997[107]	112	Yes	0/0	Yes		X	X	X	X		X
Majewski 2000[71]	73	?	?	?	X						X
Möller 2001[84]	112	No	1/1 1	Yes	X	X	X	X	X	X	X
Twaddle 2007[132]	42	Yes	2/1	No			X	X	X	X	X
Metz 2008[78]	83	Yes	3/5	Maybe			X	X	X	X	X
Willits 2010[141]	144	Yes	2/3	No				X	X	X	X
Nilsson-Helander 2010[87]	79	Yes	2/6	No				X	X	X	X
Keating 2011[55]	80	Yes	2/4	No				X			
Olsson 2013[92]	100	Yes	0/5	Yes							
RR-rate (operative vs. non-operative)					3% vs. 13%	4% vs. 13%	5% vs. 12%	4% vs. 10%	4% vs. 11%	4% vs. 9%	RR 0.4
Infection-rate (operative vs. non-operative)					5% vs. 0%	4% vs. 0%	4% vs. 0%	3% vs. 0%	4% vs. 0%	2% vs. 0%	NA
Total complication rate (other than RR)					NA	34% vs. 3%	29% vs. 8%	27% vs. 7%	27% vs. 6%	NA	RR 3.9

***Table 1**: RCT's (Y-axis) and meta-analyses (X-axis) comparing operative and non-operative treatment of acute Achilles tendon rupture. The left side of the table shows the individual RCT's conclusions. The right side of the table shows the meta-analyses, which studies they included and their overall conclusion. No=Number of patients, RR=Re-rupture, Rec=Recommend. (*) operative / non-operative. Modified after Tengberg et al.[126] and Olsson[93].*

Most of the trials published before 2005 suggested better outcome after surgery due to a higher rate of re-rupture in the non-surgical group[23,84,107]. Since then a number of high quality RCT's have opted in favor of non-operative treatment due to a non-significant difference in the rate of re-rupture and a significantly increased risk of other complications in the surgically treated

group[55,87,132,141]. In the same period two large prospective cohort studies looking at 945 and 487 patients, respectively, showed re-rupture rates of 2.8% and 6.6% in non-operatively treated patients[11,136]. Looking at the meta-analyses we find compelling evidence that operative treatment yields a risk of re-rupture of 3-5% and non-operative treatment of 9-13%. Likewise operative treatment yields a risk of other complications of 27-34% and non-operative treatment of 3-8%. Looking at functional results some RCT 's have been able to show a slightly improved function after operative treatment[23,87], but this is not reflected in the meta-analyses[48,49,57,117,139].

3.2 Mobilization vs. Immobilization

The role of mobilization has been discussed since the early 1980s and has gained increasing popularity over the past decade[8,27,74,80,104,122,132]. All RCT's comparing operative and non-operative treatment published after 2007 have used mobilization in both study groups. In 2007 Twaddle & Poon hypothesized that use of mobilization might be the most important factor in optimizing outcome in patients with Achilles tendon rupture and that surgery makes no difference to the outcome apart from increasing the risk of local infection[132].

Looking at the literature very little evidence exists concerning the use of mobilization in the treatment of acute Achilles tendon rupture. The shift towards mobilization has been driven by RCT's comparing operative and non-operative treatment protocols and not by trials comparing mobilization and immobilization[55,78,87,92, 117,132, 141]. The low rate of re-rupture in both the operatively and non-operatively treated groups has been attributed to the early controlled rehabilitation regimes, though this has not been the research area of the trials.

In order to investigate the effect of mobilization one should look at trials designed for this purpose. Operatively treated and non-operatively treated patients must be investigated separately, as the baseline situation for the healing process is different. Also controlled early motion must be distinguished from controlled early weight-bearing, as it is unknown how the two variables affect tendon healing and how they interact.

3.2.1 Controlled early motion

Three RCT's have investigated the effect of controlled early motion in the treatment of acute Achilles tendon rupture (table 2)[24,51,80]. The quality of the three trials was assessed to be medium

by two independent reviewers using the Jadad score[47,90]. No statistically significant differences were found in rate of re-rupture and other complications between the immobilized group and the group treated with controlled early motion. The studies argue for shorter sick leave, less tendon elongation, and better strength in the group treated with controlled early motion.

Trials	Jadad score	No of patients	Treatment	Weight-bearing	Re-rupture Motion/Immobilization	Other complications Motion/Immobilization
Cetti 1994[24]	3	60	Operative	No	1/2	1/6
Mortensen 1999[80]	3	71	Operative	No	1/2	1/0
Kangas 2003[51]	2	50	Operative	Yes	1/2	?

***Table 2**: Table showing RCT's comparing controlled early motion and immobilization.*

3.2.2 Controlled early weight-bearing

One RCT has investigated the influence of controlled early weight-bearing in the treatment of acute Achilles tendon rupture (table 3)[121]. The study looked at health-related quality of life assessed with use of the RAND 36-Item Health Survey (RAND-36) as its primary outcome. Secondary outcomes were activity level, calf strength, ankle range of motion, return to sports and work, and complications. 98 patients (89%) completed the six-month follow-up. At six weeks the weight-bearing group had significantly better scores than the non-weight-bearing group in the RAND-36 domains of physical functioning, social functioning, role-emotional, and vitality scores ($p<0.05$). Patients in the weight-bearing group also reported fewer limitations of daily activities at six weeks postoperative ($p < 0.001$). At six months, no significant differences between the groups were seen in any outcome. Suchak et al. concludes that no detrimental effect of weight-bearing from the second postoperative week was found in operatively treated patients.

Trials	Jadad score	No of patients	Treatment	Motion	Re-rupture Motion/Immobilization	Other complications Motion/Immobilization
Suchak 2008[121]	3	110	Operative	Yes	0/0	8/11

***Table 3**: Table showing RCT's comparing controlled early weight-bearing and immobilization.*

3.2.3 Controlled early motion and weight-bearing

Three RCT's have investigated the combined influence of controlled early motion and weight-bearing in the treatment of acute Achilles tendon rupture (table 4). Saleh et al.[104] developed a new

orthosis, the Sheffield splint, allowing both controlled early motion and weight-bearing which they tested against immobilization in cast. They found that the group treated with mobilization regained mobility and range of motion significantly quicker than the immobilized group. Costa et al.[27] also tested a new orthosis allowing both controlled early motion and weight-bearing against immobilization in cast. No significant differences were found. The trials were influenced by selection bias, as active people were operated and inactive people were treated non-operatively.

Trials	Jadad score	No of patients	Treatment	Re-rupture Motion/Immobilization	Other complications Motion/Immobilization
Saleh 1992[104]	1	40	Non-operative	1/1	?
Costa 2006[27]	3	48	Non-operative	1/2	0/2
Costa 2006[27]	3	48	Operative	2/0	6/7

***Table 4**: Table showing RCT's comparing the combined influence of controlled early motion and weight-bearing against immobilization.*

3.3 Rehabilitation protocols

The following are examples of rehabilitation protocols being used after both operative and non-operative treatment of acute Achilles tendon rupture:

3.4.1 Immobilizing rehabilitation protocols

A typical immobilizing treatment protocol has been described by Cetti et al.[23]: A below-the-knee plaster cast with the foot in 20° of plantar flexion is worn for eight weeks. During this period no weight-bearing is allowed on the injured leg. After eight weeks the cast is removed and weight-bearing allowed. Alternatively the cast is changed after three to four weeks bringing the ankle in a neutral position or a brace is worn throughout the treatment period gradually bringing the ankle into neutral position.

3.4.2 Mobilizing rehabilitation protocols

Mobilizing treatment must be divided into 1) controlled early motion, 2) controlled early weight-bearing and 3) controlled early motion and weight-bearing.

3.4.2.1 Controlled early motion

Controlled early motion can be performed using a dynamic brace, allowing movement of the ankle, or using a removable brace, instructing the patient to remove the brace and exercise. A

treatment protocol using a dynamic brace has been described by Nilsson-Helander et al.[87]: Patients are treated with a below-the-knee cast with the foot in equinus position for two weeks, followed by an adjustable brace for the next six weeks. The brace is set at free plantar flexion motion with dorsiflexion limited to -30° the first two weeks, -10° the next two weeks, and +10° the last two weeks. Weight-bearing as tolerated is allowed after six to eight weeks.
A treatment protocol using a removable brace has been described by Twaddle et al.[132]: Patients are treated with a removable brace for eight weeks. The foot is initially placed in equinus position by application of three wedges. Every second week a wedge is removed, slowly bringing the ankle to neutral. Patients are instructed to remove the brace for five minutes of every hour and, while sitting with the injured leg hanging, practice active ankle dorsiflexion and passive plantar flexion, letting the foot fall down as far as was comfortable. Particular emphasis was made of the importance of not dorsiflexing the ankle beyond the neutral position and remaining non-weight-bearing.

3.4.2.2 Controlled early weight-bearing

Controlled early weight-bearing without movement of the ankle is a widely used treatment protocol in Scandinavia[8]. Yet, it has not been possible to find a published description of this protocol. The following treatment protocol is used in hospitals in the area of Copenhagen: The patient is treated with a brace for six weeks when operatively treated and eight weeks when non-operatively treated. The foot is initially placed in equinus position by application of wedges in the brace and slowly brought to neutral by removal of the wedges. Full weight-bearing is allowed from day one.

3.4.2.3 Controlled early motion and weight-bearing

A treatment protocol using both controlled early motion and weight-bearing has been described by Möller et al.[84]: The patient is treated with a below-the-knee plaster cast with the ankle in equinus for two weeks. After two weeks the cast is replaced with a brace and full weight-bearing and range of motion exercises are encouraged during weeks three to eight.

4 Outcome assessment

'If you can measure that of which you speak, and can express it by a number, you know something of your subject, but if you cannot measure it, your knowledge is meager and unsatisfactory.'

William Thomson

Outcome denotes whether or not a patient benefits from the medical care provided[37]. In order to evaluate patient outcome and compare treatment regimens valid, broadly accepted and clinically relevant outcome parameters are required.

4.1 Patient reported outcome measures

Patient reported outcome measures (PROM's) have added a new dimension to clinical outcome evaluation. PROM's are important both for assessing individual patients in the clinic, for quality monitoring and research purposes. Traditional clinical methods for assessing outcome after Achilles tendon rupture may fail to detect the patient's perception of disability[33,38,55,88,123]. Over the past decades numerous PROM's have been developed, but only the Achilles tendon Total Rupture Score is developed and validated for use after acute Achilles tendon rupture[54]. The most widely used scores are presented in the following paragraphs.

4.1.1 Achilles tendon Total Rupture Score (ATRS)

The Achilles tendon Total Rupture Score consists of 10 items reflecting symptoms and physical activity after treatment of acute Achilles tendon rupture. The items are assessed using a Likert scale (range 0-10; 10 being the best possible score). It was developed and validated in 2007 by Nilsson-Helander et al.[88] It has since been translated to English and Danish and both versions have been validated[33,53]. The ATRS was found to be a good and reliable PROM for measuring differences of more than 7 points between groups of patients. However, for assessing individual patients in the clinic, the ATRS showed serious limitations, as it cannot be expected to detect changes of less than 19 points when reassessing individual patients at several points[33].

4.1.2 Victorian Institute of Sports Assessment – Achilles (VISA-A)

The VISA-A questionnaire is a PROM validated for Achilles tendinopathy based on symptoms. It consists of eight questions that measure the domains of pain, function in daily living and sporting activity. The results range from 0 to 100, where 100 represents the ideal score[103]. VISA-A has been used in validations of the ATRS[88,53] and has been translated to and validated in Danish[46].

4.1.3 Physical Activity Scale (PAS)

The physical activity scale has been developed to be a simple alternative to measuring physical activity by diary. It is a self-reported questionnaire estimating the total physical activity on an average week-day. It is developed and validated in Danish[146].

4.1.4 Health related quality of life

A wide range of patient reported questionnaires to assess quality of life have been developed and validated. The most widely used are listed below this paragraph. Inspired from those a purpose made questionnaire was developed to investigate the health related quality of life during the initial eight weeks of treatment in study II (Annex A). Five items were assessed using a Likert scale (range 0-10; 10 being the best possible score). The items reflected: 1) limitations in daily living, 2) limitations in work situations, 3) limitations in social life, 4) affection of the patient mood, and 5) level of pain.

4.1.4.1 Short Form 36 (SF-36) and RAND-36

The SF-36 and RAND-36 are identical multi-purpose, short-form health surveys containing 36 questions[39,124,138]. They measure eight health concepts summarized in two main scores: the physical component score and the mental component score. The questionnaires are thoroughly tested and validated[39,124,138].

4.1.4.2 EuroQOL (EQ-5D)

The EQ-5D essentially consists of a descriptive system comprising five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale where the person is to give an overall rating of self-rated health[127]. The questionnaire is thoroughly tested and validated[97].

4.2 Functional testing

Functional testing is widely used in trials assessing the outcome after acute Achilles tendon rupture.

4.2.1 Heel-rise test

The heel-rise test is an endurance test where the number of standing unilateral heel raises, at a rate of 40/minute, is counted. Only heel lifts above 5 cm are counted[83,85].

4.2.2 Heel-rise work test

The heel-rise work test is an endurance test where the patient stands on one leg and lifts the heel up and down until exhaustion. The participants are allowed to place two fingertips per hand, at shoulder height, against the wall for balance. A frequency of 30 heel-rises per minute is kept. The participants are instructed to go as high as possible on each heel-rise and then lower the heel to the starting position before next heel-rise. The participants are asked to perform as many heel-rises as possible. The test is terminated when the patient stops, cannot maintain the frequency, or does not perform a proper heel-rise (<2cm)[114].

Silbernagel et al. have found a good validity of the heel-rise work test and greater ability to detect differences between the injured and the uninjured sides compared to the heel-rise test[114].

4.2.3 Heel-rise height

The heel-rise height is measured under the same setting as the Heel-rise work test. The maximum heel-rise is recorded[114]. The decrease in heel-rise height has been hypothesized to be correlated to tendon lengthening[115].

4.2.3 Single heel-rise test

The patient stands with the foot in neutral position. It is recorded whether the patient is able to make a single heel-rise on the injured leg. The heel-rise is acknowledged if the heel can be lifted at least 2 cm with stretched knee. It has been shown that the ability to do a heel-rise 12 weeks after rupture is correlated to outcome. The heel-rise ability appears to be an important early achievement and reflects the general level of healing, which influences patient-reported outcome and physical activity[91].

4.2.4 Strength tests

Strength testing has been performed in different settings. Sibernagel et al. had the patients do concentric and eccentric toe-raise against increasing weight[113]. Möller et al. tested concentric and eccentric strength with the patient sitting with 90 degrees flexion in the hip and knee using an isokinetic dynamometer. Angular velocities of 30°/sec and 180°/sec were used. The reliability was found to be good[83]. McNair et al. tested concentric strength at an angular velocity of 240°/sec[76].

4.2.5 Jump tests

In 2005 Silbernagel et al. described a test battery consisting of three jump tests: a counter movements jump, a drop counter movement jump and hopping[113]. The test battery was found to be reliable and able to detect differences in lower leg function between the injured and non-injured limb[87,113].

4.3 Biomechanical testing

Biomechanical testing is typically done using an isokinetic dynamometer[76,83]. The patient is seated or lying with the hip and knee joint in a specified position. Positions between 0 and 90 degrees have been described for each joint[76,83]. The subjects foot is strapped to the pedal of the dynamometer and he/she is asked to relax and not activate the lower limb muscles while the isokinetic dynamometer moves the ankle joint in dorsiflexion at an angular velocity of typically 5˚/sec[76,83]. The resistant torque is sampled by the isokinetic dynamometer and the matching torque and angle values are recorded.

4.3.1 Stiffness

Stiffness is the slope of the stress strain curve. Stiffness of the plantar flexor muscle-tendon complex increases with increasing dorsiflexion. It is, therefore, often reported in intervals like early, middle and late dorsiflexion[76].

4.3.2 Peak passive torque

Peak passive torque is the maximum torque exerted when stretching the passive ‘plantar flexion muscle-tendon complex’[18,76]. It is usually reached in maximum dorsiflexion.

4.3.3 Energy stored during loading

The energy stored during loading is the area under the loading curve. It represents the energy absorbed by the plantar flexor muscle-tendon complex[76].

4.3.4 Torque relaxation

The torque relaxation is representative of the shock absorbing quality of the plantar flexor muscle-tendon complex. It is the fraction of energy stored after a period of relaxation, and can be expressed as a percentage: the persisting passive torque after a period of relaxation divided by the peak passive torque[18].

4.3.5 Dissipation coefficient

The dissipation coefficient is another measure of shock absorbing quality. It is the fraction of energy released compared to the energy stored and can be calculated by dividing the energy lost in the coil-recoil process (the area between the loading and unloading curves) by the energy stored during loading (the area under the loading curve)[76].

4.4 Length measures

A variety of methods have been developed to measure Achilles tendon length and elongation[4,23,50,64,95,99,102,105,118,144]. The methods can be divided into four groups depending on modality: clinical, X-ray, ultrasound (US), and Magnetic Resonance Imaging (MRI).

4.4.1 Clinical

Clinically, the length of the Achilles tendon can be estimated by the spontaneous position of the ankle joint in the relaxed leg (figure 10). An Achilles tendon of normal length positions the ankle joint in 10-20 degrees of plantar flexion when the patient is lying prone with the knees flexed 90 degrees. An elongation of the tendon will make the foot fall into neutral or dorsiflexion[72].

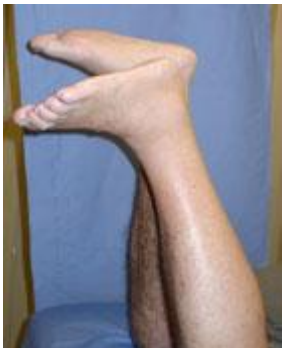

***Figure 10**: Matles test*

Likewise, the height of a maximal heel-rise has been used to estimate elongation of the Achilles tendon[91,115].

4.4.2 Radiological

X-ray allows for measurement of displacement of the torn tendon ends by implantation of radiological markers (figure 11)[23,50]. The latest and best validated method is Roentgen Stereophotogrammetric Analysis (RSA) using tantalum beads as markers[64,105]. Implantation of the markers is invasive and so far the technique has only been used to evaluate elongation after operative treatment.

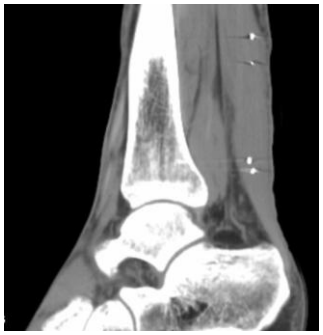

***Figure 11**: RSA markers implanted in the Achilles tendon*

4.4.3 Ultrasound

Ultrasound (US) has been established as an important and cost-effective tool in the diagnosis of tendon problems. It provides a fast investigation that can be performed by the surgeon. Three types of US based length measures have been described for the Achilles tendon.

Rees et al. developed a method combining video-based motion capture and US imaging[102]. Achilles tendon length was defined as the distance between the gastrocnemius muscle tendon junction and the tendon insertion at the calcaneus. Two retroreflective markers were placed on the back of the US probe and the markers were used to track the position of the probe. The measurement was validated by Silbernagel et al.[115] It showed high reproducibility and a measurement error of < 1%.

Panoramic ultrasound imaging allows the transducer to be moved along the patients Achilles tendon, blending multiple images together to form one long image with an extremely wide field of view[99] (figure 3). The method is easy to perform and clinically applicable, but no validation of the measurement has been published[95,118,144]. The authors of study IV have tested reliability of the measurement in a setting similar to the one used in study IV. The data has not been published yet, but showed an average intra-rater reliability of ICC 0.84, SEM 0.94 and MDC 2.62 and inter-rater reliability of ICC 0.89, SEM 0.78 and MDC 2.15.

Finally, Amlang et al. reported an US classification system to be used for individual treatment selection in patients with acute Achilles tendon rupture, looking at the degree of overlap of the

torn tendon ends as a surrogate for tendon displacement and elongation[4]. This classification system is yet to be validated and correlated to the final outcome of treatment.

4.4.4 MRI

Magnetic Resonance Imaging (MRI) is also a non-invasive modality for tendon length measurement[60]. In relation to US the setup is more demanding and expensive, as radiological assistance is needed to perform MRI measurements.

4.4.5 Strength in plantar flexion

Strength in the terminal part of plantar flexion can be used as a surrogate for tendon elongation. If tendon elongation is present one would expect strength to decline as plantar flexion increases and the suralis muscle loses its ability to contract further.

4.5 Complications

All published RCT's have reported the rate of complications[23, 55,84,87,107,132,141]. Some studies have reported all complications and others only selected complications.

4.5.1 Re-rupture

The rate of re-rupture is the most common primary endpoint in the literature[23, 55,84,87,107,132,141]. However, a clear definition of how re-rupture is defined is seldom given.

4.5.2 Infection

Infections can be divided into superficial and deep infections. Superficial infections are related to the skin, whereas deep infections involve the Achilles tendon.

4.5.3 Other complications

Other reported complications involve damage to the suralis nerve, adhesions between the tendon and the surrounding connective tissue, scar problems and deep vein thrombosis[79,94].

4.6 Return of function

In 2006 Costa et al.[27] concluded that the return to normal activities was the most important outcome measure as viewed by the patient and therefore claimed that it also should be the most important outcome measure for researchers.

4.6.1 Sick leave

The length of sick leave is of fundamental importance for the patient as well as for society. The measurement is usually self-reported through questionnaires or structured questioning at follow up[27,84].

4.6.2 Return to sport

Most acute Achilles tendon ruptures are acquired through sporting activities. The return to sports, and preferably a level of sporting activity similar to the one before the injury, is therefore an obvious outcome. The measurement is usually self-reported through questionnaires or structured questioning at follow up[23,57].

4.7 Validity, reliability and agreement of measurements

Valid and reliable outcome parameters are cornerstones in proper research. Invalid outcome parameters may lead to wrong conclusions and unreliable outcome parameters may keep actual differences from being detected. Terminology within the field is confusing and imprecise, as it differs between papers and textbooks[14, 44,52,62,123,133]. The following chapter is an outline of the terminology and concepts as they are understood and used in this thesis.

4.7.1 Validity

Validity can be divided into content, criterion and construct validity. Further description of this subdivision is out of the scope of this thesis. Generally speaking validity is the extent to which a measurement measures what it claims to measure (figure 12).

4.7.2 Assessment of validity

In order to assess if a measurement instrument actually measures what it claims to measure, one needs to know the real value of the object being measured. For example, if one would like to assess if an ultrasound measurement measures distances of tendons correctly, one needs to know the actual length of the measured tendons. If the actual length is not known, an alternative is to define a gold standard of measurement to validate the new measurement against. Validity can be expressed as the measurement error[115]:

$$Measurement\ error = \frac{\text{Actual length} - \text{meassured length}}{\text{Actual length}}$$

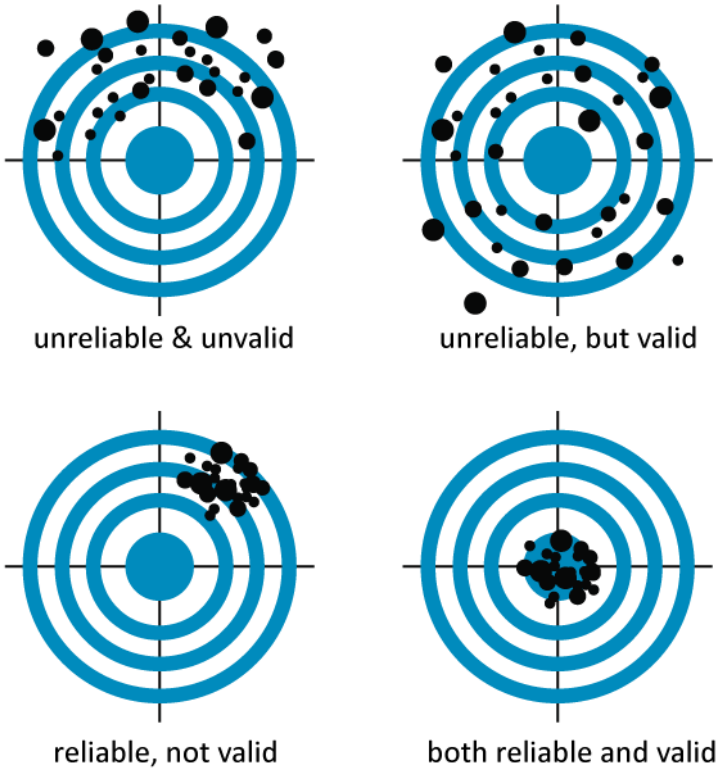

***Figure 12**: Diagram showing the difference between validity and reliability. (modified from Nevit Dilmen)*

4.7.3 Reliability and agreement

The term reliability, as used in the previous chapter (4.7.1), refers to the spread of data. It can be further subdivided into the terms reliability and agreement[133]. Agreement is the extent to which a measurement measures the same at different occasions; it is related to the measurement error of the measurement itself. Reliability is the extent to which study objects can be distinguished from each other, despite measurement errors; it relates the measurement error of the measurement to the natural variability of the study population[62,133].

***Figure 13**: Diagram showing the difference between reliability and agreement. (Modified from de Vet et al. 2006)*

Figure 13 illustrates an example of 3 subjects (●, ■ and △) being measured five times. The distance between the five identical symbols represents the agreement of the measurement (the measurement error), which is not affected by the variability of the population. In contrast, reliability of a measurement is influenced by the variability of the study population. In a population represented by the subjects ● and ■ the measurement will have a good reliability, as the measurement error will not affect discrimination of the subjects. In a population represented by the subjects ■ and △ the measurement will have a poor reliability, as the measurement error will affect the ability to discriminate the subjects. Reliability is a characteristic of the performance of an instrument in a certain population sample. Agreement is rather a characteristic of the measurement instrument itself[133].

4.7.4 Assessment of agreement and reliability

4.7.4.1 Kappa-statistics

Agreement between categorical data is often assessed using kappa-statistics. The kappa-value tells the observed agreement as a percentage of agreement expected just by chance. A value of 1 indicates perfect agreement and a value of 0 indicates no agreement[2].

4.7.4.2 Intraclass correlation coefficient (ICC)

Reliability of a measurement can be assessed using the Intraclass Correlation Coefficient (ICC). The basic formula of the ICC is:

$$Reliability = \frac{\text{Variability between study objects}}{\text{Variability between study objects} + \text{Measurement error}}$$

If the measurement error is small, compared to the variability between persons, the ICC approaches 1. This means that the discrimination of the persons is hardly affected by the measurement error, and thus the reliability is high. If the measurement error is large, compared to the variability between persons, the ICC value becomes smaller[133].

4.7.4.3 Standard error of measurement (SEM) and minimal detectable change (MDC)

Agreement of a measurement can be assessed by calculating the standard error of the measurement (SEM) and the minimal detectable change (MDC). The SEM is used to assess the

agreement between groups of data. It can be derived from the ICC: SEM = standard deviation x √(1 – ICC)[133]. The MDC is used to assess agreement between data of the individual subjects. It can be derived from the SEM: MDC = 1.96 x √2 x SEM. Agreement parameters are expressed on the actual scale of measurement, and are therefore easily interpretable[133].

4.7.4.4 The Bland-Altman method

Agreement can be assessed graphically using the Bland-Altman plot[14,15]. The plot shows the difference between measurements plotted against the average of measurements (figure 14). The mean shows if there is a systematic difference between measurements and the 95% limits of agreement show the spread of data in the sampled distribution. The limits of agreement are calculated as the mean ± 1.96 standard deviations. The visual presentation of data makes it possible to detect skewed distributions and correlation between measurement error and the scale of the measurement.

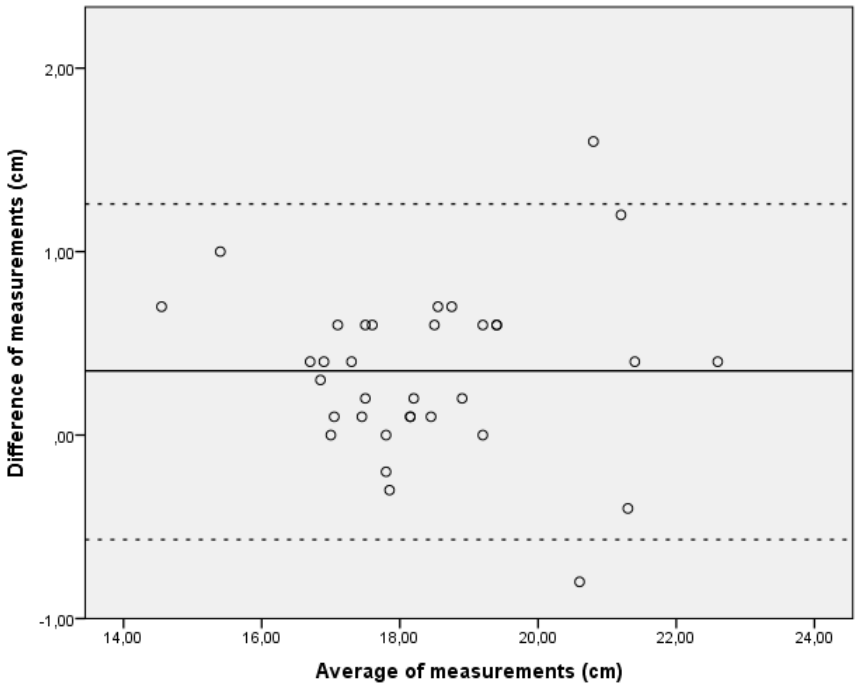

***Figure 14**: Bland-Altman plot showing difference against mean*

5 Aims

Aim at the sun, and you may not reach it; but your arrow will fly far higher than if aimed at an object on a level with yourself.

Joel Hawes

Over the past decade a change in treatment of acute Achilles tendon rupture away from operative and immobilizing treatment towards non-operative treatment using controlled early motion occured[8,74]. This thesis addresses the question: 'What is the optimal non-operative treatment protocol for acute Achilles tendon rupture?'

5.1 Aim of the thesis

The aim of this PhD thesis was to evaluate non-operative treatment of acute Achilles tendon rupture, in order to pave the way for national and international treatment guidelines concerning acute Achilles tendon rupture.

5.2 Aims of the studies

5.2.1 Study I: Treatment of acute Achilles tendon rupture in Scandinavia

The aim of this survey was to investigate whether departments treating acute Achilles tendon rupture in Scandinavia adhere to the latest evidence.

5.2.2 Study II: The influence of early weight-bearing on clinical outcome

The aim of this blinded, randomized, controlled trial was to compare patient reported and functional outcome in patients randomized to immediate weight-bearing or non-weight-bearing in a non-operative treatment protocol for acute Achilles tendon rupture using controlled early motion.

5.2.3 Study III: The influence of early weight-bearing on biomechanical outcome

The aim of this blinded, randomized, controlled trial was to compare the biomechanical properties of the plantar flexor muscle-tendon complex of both limbs in patients randomized to early weight-

bearing or non-weight-bearing. Both groups were treated non-operatively using controlled early mobilization.

5.1.4 Study IV: A Novel Ultrasound Measurement of Achilles tendon Length and Elongation

The aim of this study was to develop and validate a method which can determine Achilles tendon length and elongation accurately in a clinical setting using standard US equipment. In order to do so we had the following specific aims:

1) US identification of the anatomical landmarks and development of the specific measurement
2) Assessment of the intra-rater reliability
3) Assessment of the inter-rater reliability
4) Assessment of the validity by comparison with MRI
5) Comparison of the tendon length of both legs of the same subject

6 Subjects and methods

'I hate definitions!'

Benjamin Disraeli

In this chapter the methodology used in study I-IV is described. Outcome parameters and statistical methods are discussed and critically assessed. A thorough discussion of methodological considerations is done in chapter 7.

6.1 Study design, subjects, material and ethical considerations

6.1.1 Study I: Treatment of acute Achilles tendon rupture in Scandinavia

6.1.1.1 Study design

The study was conducted as a questionnaire based cross-sectional study investigating: 1) the use of surgical treatment, 2) the use of dynamic rehabilitation, and 3) the use of weight-bearing.

6.1.1.2 Subjects

All orthopedic departments treating acute Achilles tendon rupture in Denmark, Sweden, Norway and Finland were identified. Only public hospitals were included as private hospitals according to the experience of the authors play a negligible role in treatment of acute Achilles tendon rupture in Scandinavia. Data were collected in the period from October 2011 to October 2012.

6.1.1.3 Material

A questionnaire was developed in Danish and translated by bilingual speakers into Swedish, Norwegian and Finish (Annex B). The questionnaire was divided into four parts. Part one investigated Achilles tendon rupture diagnostics, how choice of treatment was made and to what degree the patients were involved in the decision making process (four questions). Part two investigated which patients were recommended surgical treatment, which surgical technique was used and what kind of post-surgical regimen was offered (seven questions). Part three investigated what kind of non-surgical treatment was offered (three questions). Part four consisted of three patient cases where preference of surgical or non-surgical treatment had to be chosen.

6.1.1.4 Ethical considerations

Our survey did not make use of patients or animals and as such no ethical consideration were made in regard to those.

6.1.2 Study II: The influence of early weight-bearing on clinical outcome

6.1.2.1 Study design

This was a blinded, randomized, controlled, superiority trial with participants individually randomized to one of two parallel groups. The trial was designed in accordance with the Consort requirements; no changes were made to the trial design after commencement of the trial.

6.1.2.2 Subjects

Sixty patients were included in the trial. Patients with acute Achilles tendon rupture referred to the orthopedic department of Copenhagen University Hospital Hvidovre from April 2011 to March 2012 were assessed for eligibility. Diagnosis was based on a medical history with a clear snap of the Achilles tendon and a clinical examination with a palpable gap and positive Thompsons test[130].

All patients aged 18 to 60 years who were expected to be able to follow the treatment protocol and give written consent in Danish were eligible for inclusion if randomization could be done within 4 days of the rupture. Exclusion criteria were previous Achilles tendon injury, corticosteroid injections within the last 6 months, ASA-score of three or more, medical history of arterial insufficiency in the legs and rupture within 1 cm of calcaneus.

29 patients from the intervention group and 27 from the control group were included in the one-year analysis, all belonging to their original assigned groups. The groups were comparable at all parameters except for height with the non-weight-bearing group being three cm taller.

6.1.2.3 Material

All patients were treated with controlled early motion and randomized to either immediate weight-bearing or non-weight bearing.

<u>Intervention</u>

The intervention group was allowed full weight-bearing from day one. Crutches were recommended but not obligatory the first two weeks of treatment. The control group was

instructed not to bear weight for the first six weeks of treatment. The last two weeks full weight-bearing was allowed

Standard treatment protocol used in both groups

In the emergency department an ankle orthosis (DJO Nextep Contour2 Walker) with three wedges of 1.5cm was applied, fixating the ankle in equinus position (20-30 degrees of plantar flexion). The orthosis was worn for eight weeks gradually bringing the ankle to neutral position by removing a wedge every second week (table 5).

Table 5: Treatment protocol

Week 1 and 2
Orthosis with three wedges.
The orthosis could not be removed at any time.
Intervention group: Weight-bearing allowed, crutches were recommended.
Control group: No weight-bearing.

Week 3 and 4
Orthosis with two wedges.
Controlled early motion in both groups.
Intervention group: Full weight-bearing.
Control group: No weight-bearing.

Week 5 and 6
Orthosis with one wedge.
Controlled early motion in both groups.
Intervention group: Full weight-bearing.
Control group: No weight-bearing.

Week 7 and 8
Orthosis without wedges.
Controlled early motion in both groups.
The orthosis could be removed at night.
Intervention group: Full weight-bearing.
Control group: Full weight-bearing.

Week 9 to 16
Visit to physiotherapist three times a week.
Standardized rehabilitation protocol with room for individualization

Patients were seen in the outpatient clinic after two and eight weeks. The patients were instructed not to remove the orthosis at any time during the first two weeks. After two weeks the first wedge was removed and controlled early motion begun: Patients were instructed to remove the orthosis

at least five times a day sitting on the edge of a table with both legs hanging (figure 15). Gravity plantar flexed the foot and the patient actively dorsiflexed the foot to a horizontal position. Patients were instructed to do this in series of 25 repetitions. The orthosis was not to be removed inbetween exercises from week three to six. The last two weeks of treatment the orthosis could be removed at night.

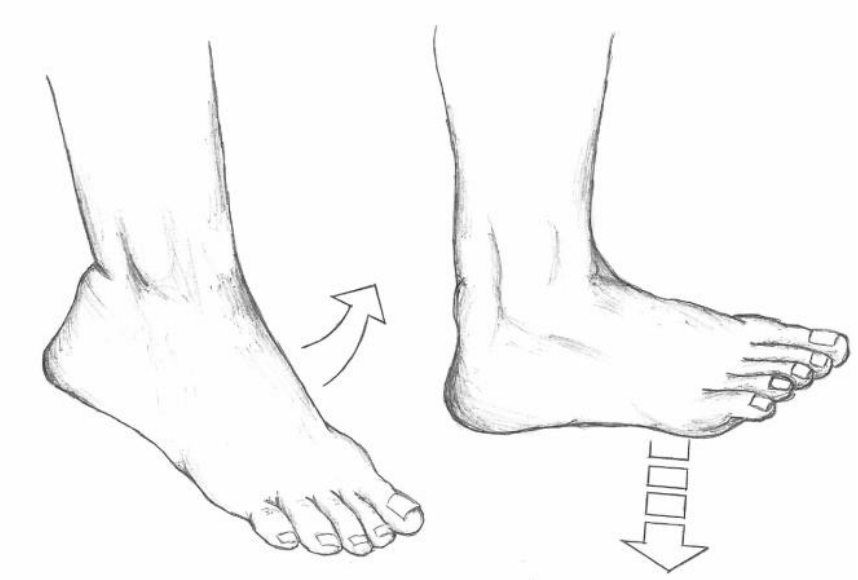

***Figure 15**: Controlled early motion. Gravity plantar flexed the foot, where upon the patient actively dorsi flexed the foot to a horizontal position. Patients were instructed to do this in series of 25 repetition five times a day. Drawing by Ilija Ban, MD*

6.1.2.4 Ethical considerations

We believe that the potential benefits for the patients enrolled in the study (better functional outcomes, improved health-related well-being and economic savings) exceed the potential inconveniences (additional follow-up audits and possible risks/side effects).

The study was conducted in accordance with the principles of the Helsinki Declaration. The study was approved by the Regional Ethical Review Board. All participants received oral and written information concerning the trial before written consent was obtained. Patients were covered by Hvidovre University Hospital patient insurance.

6.1.3 Study III: The influence of early weight-bearing on biomechanical outcome

6.1.3.1 Study design

This study is based on data from a blinded, randomized, controlled trial with participants individually randomized to one of two parallel groups (study II).

6.1.3.2 Subjects

The study population was the same as described in study II (chapter 6.1.2.2). 26 patients from the intervention group and 20 from the control group were included in the one-year analysis, all belonging to their original assigned groups.

6.1.3.3 Material

The treatment protocol and the intervention was the same as described in study II (chapter 6.1.2.3). Follow up was done in the Gait analysis laboratory at Hvidovre Hospital.

Measurement of passive tension in the plantar flexor muscle-tendon complex was performed using an isokinetic dynamometer. A motor (Caldercraft Electric Motors, model 26) was driven by a DC power amplifier (model 2708; Brüel & Kjær, Naerum, Denmark) and could deliver maintained torques up to 80Nm and peak torques up to 120Nm. An electro-goniometer, connected to the footplate, measured the angle of the ankle joint and a torque meter measured the torque exerted on the footplate. This apparatus was developed and found to produce highly reproducible measurements of passive and reflex-mediated torque around the ankle joint by Sinkjær et al.[131,140]. Before testing in the isokinetic dynamometer the patient warmed up on a stationary bicycle for 5 minutes. For the measurement, the patient was positioned with the foot strapped to a pedal in 10 degrees of plantar flexion and the knee and hip fixed in 90 degrees flexion. Patients were asked to relax and not activate their calf muscles as the ankle was passively moved into dorsiflexion by the pedal at an angular velocity of 5 °/sec. The isokinetic dynamometer rested for 2 seconds at maximal dorsiflexion before the pedal was returned to the starting position at the same velocity. The resistant torque was sampled at a frequency of 1000Hz. Patients who had a ROM exciding 20 degrees of dorsiflexion were tested in the range from 10 degrees plantar-flexion to 20 degrees dorsiflexion. Seven patients had a range of motion below 20 degrees of dorsiflexion, they were tested in the range from 20 degrees plantar-flexion to 10 degrees dorsiflexion. Ten repetitions were performed on each limb. The unaffected limb was tested before the affected.

Strength was measured using the same isokinetic dynamometer setting. The patient was asked to relax as the dynamometer dorsiflexed their ankle to 10 or 20 degrees of dorsiflexion, respectively. The dynamometer rested for three seconds and the patient was encouraged to deliver maximal plantar-flexion power without activating the thigh while the dynamometer plantar flexed the foot 40 degrees from the starting position with a speed of 6.7°/s. Five repetitions were performed on

each limb. The unaffected limb was tested before the affected. Standardized verbal encouragement was provided to ensure maximal effort[77].

6.1.3.4 Ethical considerations

The ethical considerations were the same as described in study II (chapter 6.1.2.4).

6.1.4 Study IV: A Novel Ultrasound Measurement of Achilles tendon Length and Elongation

6.1.4.1 Study design

The study was done as a cross-sectional study comparing the investigated measures twice within a certain period of time.

6.1.4.2 Subjects

Both legs of 19 uninjured persons (8 males and 11 females) were studied. Their mean age was 43.4 years (SD 10.7, range 26-63). Average height was 175cm (SD 9, range 158-192) and average weight was 76.8kg (SD 12.9, range 58-110). They all had right as their dominant side.

6.1.4.3 Material

Definition of landmarks

Achilles tendon length was defined as the distance between the tendon insertion at the calcaneus and the medial gastrocnemius muscle tendon junction, as previously described by Rees et al.[102] (figure 16).

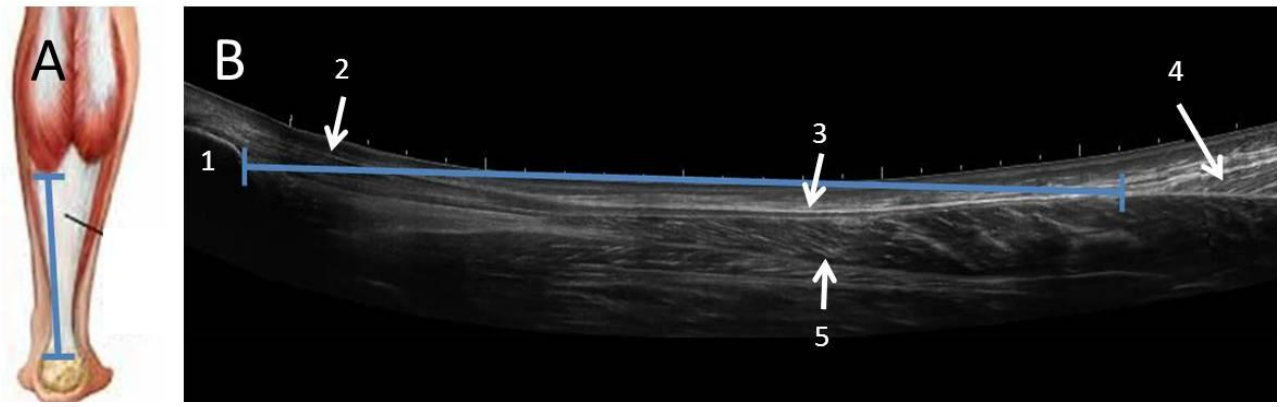

***Figure 16**: The blue line represents the distance measured by the novel ultra sound measure. (A) A posterior view of the calf. (B) A panoramic ultrasound picture of the calf: 1) Calcaneus, 2) The Achilles tendon, 3) the tendon sheet of the suralis muscle, 4) the gastrocnemius musle, and 5) the soleus muscle.*

First, the anatomical landmarks were identified and marked, then the distance between them was measured. The distal landmark was the posterior and most superior corner of the calcaneus in the midline, which on sagittal US examination was identified as the point where the cortical bone and its underlying shadow ended (figure 17). The proximal landmark was the distal tip of the medial gastrocnemius head, which was defined as the most distal point where the muscular fibers inserted into the v-shaped convergence of the deep crural fascia (figure 17).

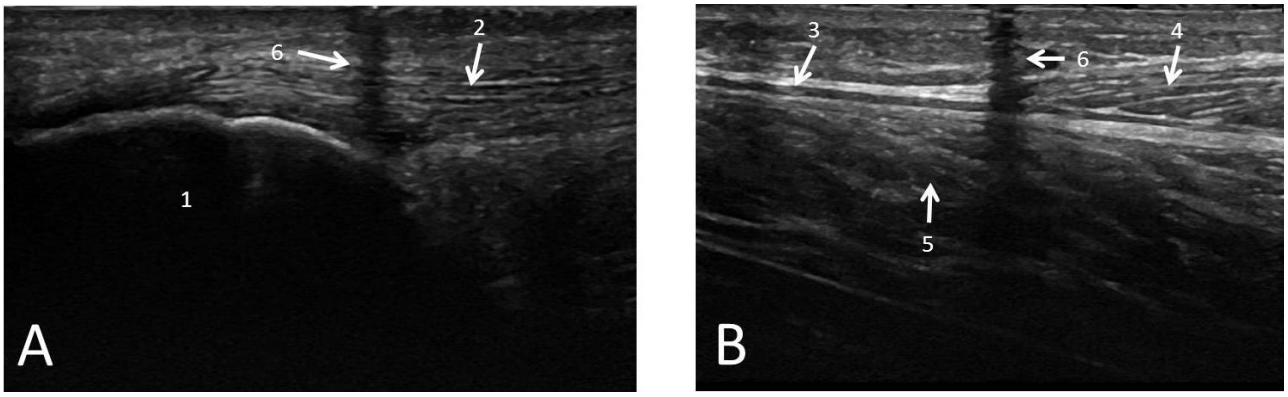

Figure 17*: Sagittal US pictures showing (A) the insertion of the Achilles tendon at the calcaneus and (B) the muscle-tendon junction. (A) The distal landmark, the posterior-superior corner of calcaneus, is seen as the point where the cortical bone and its underlying shadow ends. (B) The proximal landmark is the distal tip of the medial gastrocnemius head (the insertion of the most distal muscle fibers into the deep fascia). 1) Calcaneus, 2) The Achilles tendon, 3) the tendon sheet of the suralis muscle, 4) the gastrocnemius musle, 5) the soleus muscle, and 6) the posterior acoustic shadowing of the needle of a 21 gauge needle projecting the landmark to the skin.*

<u>Setup</u>

Participants were positioned in a prone position with the knee flexed 10 degrees. Anteriorly to (below) the ankle joint a triangle shaped foam pad was placed with the feet resting relaxed against it (figure 18). Using a goniometer the ankle joint was positioned in 10 degrees of plantar flexion by adjustment of the foam pad. Participants were positioned identically for US and MRI investigations.

The predefined anatomical landmarks were identified using longitudinal imaging. A needle was placed between the probe and the surface of the skin, and the posterior acoustic shadow created by the needle on the US image was centered over the landmark (figure 17). The position of the

needle, thus representing the landmark, was then marked on the skin (figure 18). The direct distance between landmarks was measured with a tape measure following the curves of the leg.

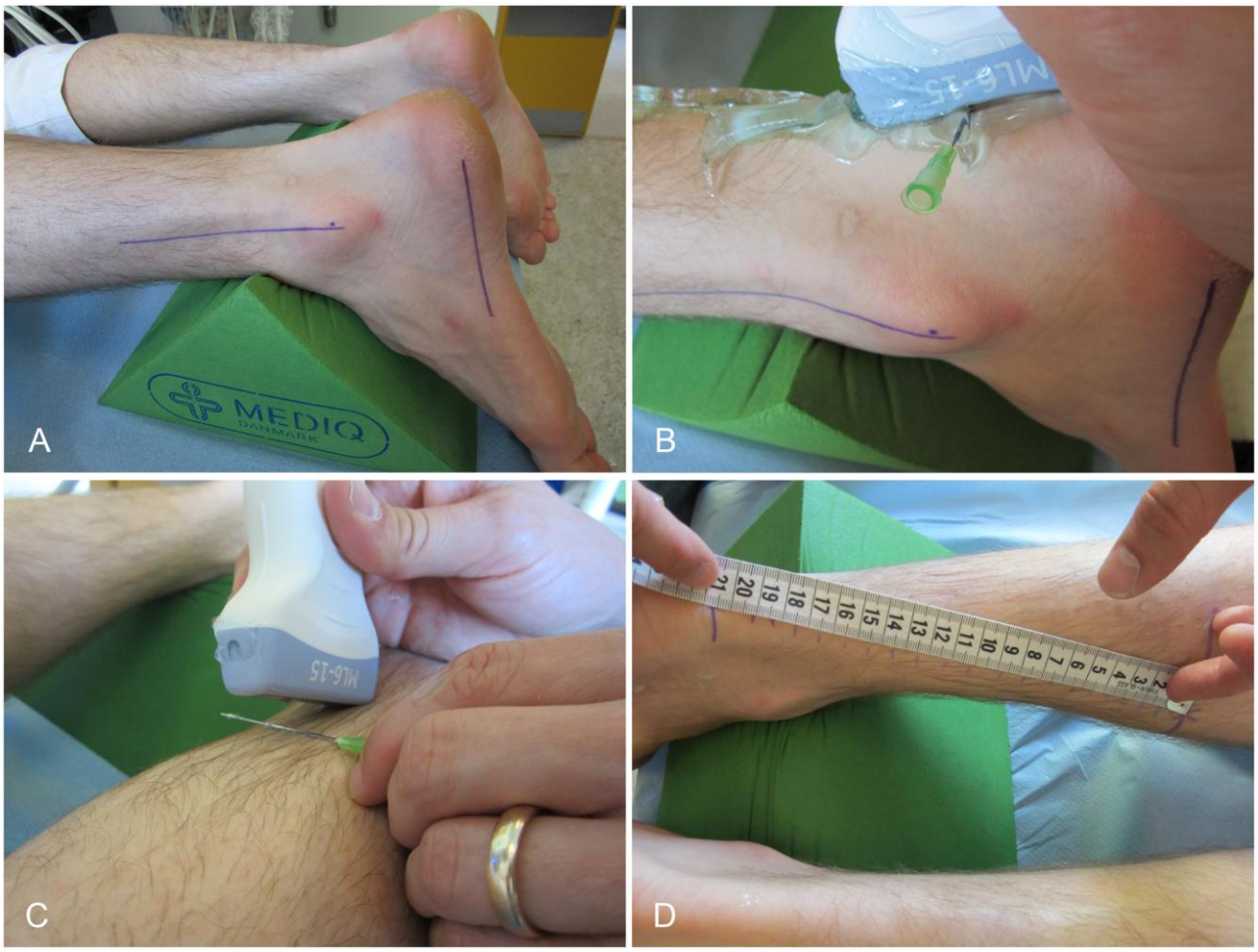

***Figure 18**: Positioning of the study subjects. Participants were positioned in a prone position with the knee flexed 10 – 20 degrees. The ankles rested on a triangular foam pad. Using a goniometer the ankle joint was positioned in 10 degrees of plantar flexion by adjustment of the foam pad (A). With a marker the point where the US probe and the needle crossed was marked on the skin (B+C). The distance between landmarks was measured with a tape measure following the curves of the leg (D).*

Reliability-testing of the US measurement was performed using three different US scanners: GE Healthcare Logiq S8, Logiq 9 and logiq P5. Frequency was set to 15 MHz and focus was dynamically adjusted by the US operator. After each scan the marks on the skin were removed in order to secure blinding of results between investigators.

The novel US measurement was validated by three independent US-investigators with two to five years of experience within musculoskeletal US. MR-images were evaluated by two independent investigators, both specialized in musculoskeletal MRI. All investigators were blinded to the results of the other investigators and to their own previous results.

Inter- and intra-rater reliability for the novel US measurement was determined for the three independent US investigators on two occasions with three weeks between scans. Within the following two months, MRI examinations were performed.

6.1.4.4 Ethical considerations

There are no known side-effects or risks associated with the performed UL and MRI investigations. We believe that the potential benefits for coming generations of patients with acute Achilles tendon rupture exceed the potential inconveniences for the study subject.
The study was conducted in accordance with the principles of the Helsinki Declaration. The study was approved by the Regional Ethical Review Board. All participants received oral and written information concerning the trial before written consent was obtained.

6.2 Critical assessment of outcomes

A variety of outcomes have been used for assessment of acute Achilles tendon rupture. The following guidelines for choosing appropriate outcomes have been suggested[37]: 1) the measure must be quantifiable, 2) the measure should be relatively easy to define and use, 3) the measure should lend itself to standardization and validation, and 4) the measure should be clinical relevant.

6.2.1 Study I: Treatment of acute Achilles tendon rupture in Scandinavia

6.2.1.1 Outcome parameters in study I

The following four outcomes were assessed in the study:

<u>1) The use of surgical treatment</u>

Departments were asked which of the following statements was most correct:

a) In principle all patients are recommended surgery
b) Healthy and active people under the age of 60 are recommended surgery

c) Active sportsmen and people with excessive demands to their Achilles tendons are recommended surgery
d) Only patients with delayed diagnosis, patients treated with corticoid-steroid, patients with sharp lesions and a few other cases are recommended surgery

2) The use of controlled early motion

Departments were asked if their treatment protocol allowed movement of the ankle joint from week three of treatment.

3) The use of controlled early weight-bearing

Departments were asked when partial and full weight-bearing was allowed.

4) The level of experience of the performing surgeons

Departments were asked if the operations were performed by specialist in orthopedic surgery or by any surgeon.

6.2.1.2 Critical assessment of the outcome parameters in study I

The chosen outcomes were investigated using a purpose made questionnaire. The questionnaire was developed in Danish and translated to Swedish, Norwegian and Finish. The Swedish and Norwegian translations were approved by the first author who is able to read and understand both languages. The questionnaire was not validated concerning construct, content or criterion validity[123]. Nor was the reliability and agreement of the questionnaire tested[62]. As such, we do not know if the questionnaire measured what it intended to measure.

6.2.2 Study II: The influence of early weight-bearing on clinical outcome

Most RCT's presented in chapter 3 have used the re-rupture rate as their primary outcome parameter. It is debatable if the re-rupture rate is a good primary outcome, as it does not contain information concerning the functional outcome and the patient's own perception of the outcome[27,33,87,121]. In 2002 Pajala et al. investigated the outcome after 23 re-ruptures and nine deep infections and concluded that the outcome after a simple re-rupture without infection is satisfactory, whereas the outcome after a deep infection often is devastating[94].

6.2.2.1 Outcome parameters in study II

We decided to follow the recommendation by Silbernagel et al.[114] and use a combination of patient reported outcome and functional outcome. Our primary outcome parameter was the Achilles tendon Total Rupture Score (ATRS) at one year follow up. Secondary outcomes were 1) the Heel-rise work test, 2) re-rupture rate, 3) length of sick leave, 4) time to return to sports, and 5) quality of life during treatment.

6.2.2.2 Critical assessment of the outcome parameters in study II

Whether to use doctor reported or patient reported outcomes is an ongoing discussion. Re-rupture and infection rate are doctor reported outcomes; they are quantifiable, easy to use and easily standardized. The ATRS is a patient reported outcome; it is quantifiable, easily standardized and relatively easy to use. The question is which of the outcome measures is the most clinical relevant.

We have chosen to use the ATRS as our primary outcome as we find the patients' perception of his/her injury to be the most important criteria of success of a given treatment. Critics of PROM-assessment argue that results are influenced by the sociocultural context, the shape and application of the questionnaire, by the patients' familiarity in answering the questionnaire and by the patients' relationship with the clinician/researcher[67,98].

The ATRS it is developed and validated for use after acute Achilles tendon rupture and found to have good validity, reliability, internal consistency and responsiveness[33,53,88]. Still, the construction of the questionnaire can be questioned. The questionnaire investigates 10 items with a possible score between zero and 10, it is thus possible to achieve a total sum score of maximum 100[88]. It is common practice in sociology and psychology to add together ordered items to sum-scores and then use these sum-scores for subsequent analyses. It is however questionable if the added item-scores represent the same value, and as such if the sum-score is a valid measurement[21]. Another problem concerning the ATRS is the lack of clear analysis guidelines. Finally, the Danish validation of the ATRS showed an SEM of 7 and an MDC of 19; meaning that differences below 7 points cannot be measured with the ATRS.

Sick leave and time-to-return-to-sport was registered retrospectively at six and 12 months follow up; though there is a risk of recall bias.

Quality of life during treatment was measured using a purpose made 5 item questionnaire. The questionnaire was not validated concerning construct, content or criterion validity[123]. Nor was the reliability and agreement of the questionnaire tested[62]. It would have added a dimension of validity to the study if a validated quality of life questionnaire had been used.

6.2.3 Study III: The influence of early weight-bearing on biomechanical outcome

No primary outcome was determined a priori as the study was based on data from study II. We did, however, suggest a primary outcome post-hoc, based on the availability of data from previous studies[18,76].

6.2.3.1 Outcome parameters in study III

We suggested peak passive torque as primary outcome parameter at one year follow up. Secondary endpoints were 1) stiffness in early, middle and late dorsiflexion, 2) energy stored, 3) torque relaxation and 3) the maximal strength.

6.2.3.2 Critical assessment of the outcome parameters in study III

The used outcome parameters have all been described and used in a range of experimental and clinical studies[17,18,76,81]. The question is, however, to what degree we are measuring the biomechanical property of the Achilles tendon and to what degree the surrounding tissue (the plantar flexor muscles, the ankle joint and the loose connective tissue) influences the measurements.

6.2.4 Study IV: A Novel Ultrasound Measurement of Achilles tendon Length and Elongation

6.2.4.1 Outcome parameters sin study IV

Intra- and inter-rater reliability and agreement was tested using the ICC, SEM and MDC. Furthermore a graphical evaluation using the Bland-Altman method was used. Validity of the novel ultrasound was tested against MRI measurements and the measurement error was calculated. Comparison of the two limbs was done using ICC, SEM and MDC.

6.2.4.2 Critical assessment of the outcome parameters in study IV

It is an ongoing discussion whether to use reliability parameters like ICC or to use the Bland-Altman method[14,62,133]. We chose to present both, which some might consider unnecessary additional material.

Proportions of agreement could have given additional information. It would have been interesting to know the proportion of measurements lying within e.g. 5mm from each other and it would be interesting to know the proportion of persons having a discrepancy between the length of the left and right Achilles tendons above e.g. 10mm.

Validity was assessed by comparing the UL-measurements with the MRI-measurements. The actual length of the tendon is not known and as such the calculated measurement error might be misleading.

6.3 Statistics

The Statistical methods used in this thesis are outlined in table 6.

6.3.1 Paper I - statistical considerations

Two-way tables with Fisher's exact test were used for analysis as cells had expected values below 5.

6.3.2 Paper II - statistical considerations

The ATRS was considered a continuous score. One could argue that it is a categorical, ordinal score, but it does not affect the statistical testing as the results were not normally distributed and the Wilcoxon signed rank test was used.

6.3.3 Paper III - statistical considerations

The paired t-test was used for evaluation within groups of data. It was also used for comparison between the right and left leg of subjects, as data from the two sides of a person were considered to be connected.

6.3.4 Paper IV - statistical considerations

The statistical considerations concerning the use of the Bland-Altman method and ICC, SEM and MDC are described in chapter 4.7.

Statistical Methods	Paper I	Paper II	Paper III	Paper IV
Type of data				
Categorical, ordinal and dichotomous	X	X	X	X
Continuous, normally distributed		X		
Continuous, not normally distributed		X		
Sample size calculation				
Made a priori		X		X
Made post hoc			X	
Comparison within groups				
Wilcoxon signed rank test *(Continuous, not normally distributed data)*		X		
Paired t-test *(Continuous, normally distributed data)*			X	
Comparison between groups				
Fischer's exact test (*Dichotomous data)*	X	X	X	
Un-paired t-test *(Continuous, normally distributed data)*		X		
Paired t-test *(Continuous, normally distributed data)*			X	
The Mann-Whitney U test *(Continuous, not normally distributed data)*		X		
Change over time				
Two way ANOVA *(Continuous, not normally distributed data)*			X	
Validity, agreement and reliability				
The Bland-Altman method				X
ICC, SEM and MDC				X

***Table 6**: Showing the statistical methods used in the four trials. The significance level for all significance tests was set to 0.05, two tailed.*

7 Methodological considerations

There are only a handful of ways to do a study properly but a thousand ways to do it wrong

Sackett

In the attempt to produce research of the highest quality, it is of outmost importance to choose the correct study design and setup in order to avoid bias and fulfill the aim of the study[2,35]. The following chapter is an attempt to 1) assess the methodological problems encountered in this thesis, 2) discuss the possible induced bias, and 3) explain how bias has been or should be controlled.

7.1 Bias

Bias refers to the presence of systematic error in the design, conduct, analysis or publication of a study[35,37,96]. More than 70 different types of bias have been described and several classification systems proposed, the most common distinguishing between information, selection and confounding bias[28,35]. Information bias refers to errors of assessment and measurement of the studied population (figure 19). Selection bias refers to factors influencing who is included in the study population. Confounding bias refers to factors that determine who is exposed to the studied intervention and influences the generalizability of the study results[35,37]. The terminology and division of bias into categories varies by discipline and among authors.

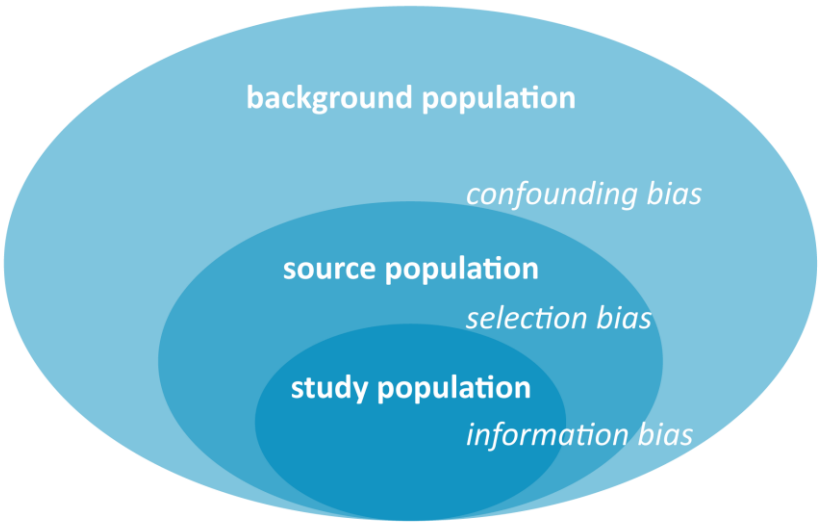

***Figure 19**: Schematic illustration of the relationship between information, selection and confounding bias and the study, source and background population. Modified from Gerhard et al.*

7.1.1 The randomized controlled trial

The RCT has been developed to produce groups who are identical in all maters except for the intervention under investigation. Ideally it would lead to unbiased conclusions.

Component	Type of bias	Description	How to control
Randomization	Selection bias	Systematic differences between baseline characteristics of the groups that are compared	Stringent randomization procedures Computer generated and concealed randomization
Blinding	Detection bias	Systematic differences between groups in how outcomes are determined	Blinding of investigators
	Performance bias	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest	Blinding of patients, health personal
Incomplete outcome data	Attrition bias	Systematic differences between groups in withdrawals from a study	Study design should consider how to avoid dropout Use of Intention to treat analysis or Available case analysis
Selective outcome reporting	Reporting bias	Systematic differences between reported and unreported findings	All outcomes are reported
Baseline imbalance	May indicate selection bias May raise questions related to effect estimate	An imbalance in baseline characteristics may indicate flaws in randomization An imbalance in prognostic factors leads to the question of whether the effect estimate is because of the treatment effect or because of the difference in prognostic factors	Stringent randomization procedures Population size above 400 Stratification for a few important prognostic factors in small trials Regression analysis to adjust for observed imbalances
Early stopping	Early stopping bias	Trials are stopped at a point when the treatment effect is high at random when an insufficient number of outcome measures have been achieved	Well defined primary endpoint and when to investigate it
Academic	Academic bias Detection	A bias towards finding the same result if the clinical trial is repeated in a new group of patients	Publication of the trial protocol Honesty concerning previous publications and convictions
Source of funding	Detection bias Performance bias Reporting bias Early stopping bias	See descriptions above. The results tend to become favorable to the sponsor's product	Declaration of source of funding

***Table 7**: Showing the main components to minimize risk of bias in RCT's proposed by the Cochrane group. Modified from Gerhard et al. 2008.*

In reality bias is always present in research studies, the question is how much bias exists and to what extend it influences the drawn conclusion[35]. The Cochrane group has published guidelines for design of RCT's in order to minimize risk of bias[41], the main components are shown in table 7.

7.2 Study I: Treatment of acute Achilles tendon rupture in Scandinavia

The aim of study I was to investigate the used treatment protocols in Scandinavia at a given time. For that an observational, prospective, cross-sectional study design was chosen, and data were collected through a questionnaire based survey. This design introduces a range of information bias.

The risk of *recall bias*; that the person who filled out the questionnaire did not recall or due to positive or negative emotions did over or under estimate the answer. It is an inherent part of a questionnaire based cross-sectional study. In order to control for recall bias a prospective design investigating the actual treatment over a given period of time could be chosen.

Also the risk of *language bias* was present. Translation and cultural differences might have led to different interpretation of the questions in different parts of Scandinavia. To better control for language bias a proper validation of the questionnaire could be made in each country. Alternatively an English questionnaire could have been used. However, it might also be differently interpreted across Scandinavia and a validation would be needed to investigate this matter.

Some of the questions were designed as ordinal scales and others as nominal scales. *Misclassification bias* might have been introduced if the scales were not intuitively understood and the questions overlapping. Again the solution to better control for misclassification bias would be a proper validation of the questionnaire.

The survey was designed to investigate the used treatment protocols in orthopedic departments across Scandinavia and did not consider the size of the respective departments. As such, the design did not allow for quantitative considerations concerning the number of patients receiving a given treatment. If one was interested in the number of patients receiving a given treatment a retrospective or prospective register study could be chosen. The prospective being the least biased of the two in this matter.

The aim of the study was to investigate the treatment in Scandinavia and as all departments in Scandinavia were included in the source population it equals the background population. Therefore no confounding bias was present. If one would like to generalize the results outside of Scandinavia an analysis of possible confounding bias should be performed.

The high response rate of 93% minimizes the risk of selection bias. Still it is possible that the remaining 7% did not respond due to a systematic difference in their treatment protocols, which would lead to unrecognized selection bias.

7.3 Study II and III: The influence of early weight-bearing on clinical and biomechanical outcome

The aim of study II and III was to investigate the effect of an intervention. For that an experimental, prospective, longitudinal design was chosen: a blinded, randomized, controlled, clinical trial. The randomized study design is the best design to prevent bias as unknown factors affecting the trial are expected to be equally distributed between groups. The randomized setup is logistically demanding and time consuming. The following is a systematic review of the components listed in table 7.

Inclusion and exclusion criteria were chosen according to existing literature. Age, delayed presentation, treatment with corticosteroid and severe medical illness were considered to be probable confounding variables and controlled for. Thus, the study can be generalized to a population of 18 to 60 year old persons without severe medical illness and without prior use of corticosteroids.

Randomization was done by the book and no selection bias was recognized. The procedure would have had more credibility if the randomization sequence had been computer generated. No baseline imbalance was found except for a small difference in height. A larger sample size would most probably have eliminated this difference.

The investigators were blinded to the intervention, whereby we have controlled for detection bias. Patients and healthcare personal could not be blinded due to the type of intervention and as such performance bias might be present. The intervention taken into consideration, it is not possible to control for performance bias as blinding of patients and healthcare personnel is not possible.

In paper II data form 56 of 60 patients were analyzed, in paper III data from 46 of 60 patients were analyzed. In order to reduce attrition bias, available-case-analysis was performed. In paper II and III it is stated that intention-to-treat-analysis was used. This is incorrect as no imputation of data was performed, only the available cases were analyzed.

All outcomes stated in the trial protocols are reported and sought published. No reporting bias was present. The trial was stopped according to the trial protocol thereby minimizing the risk of early stopping bias. The research group had no previous publication concerning the topic of interest. The risk for Academic bias is therefore low.

The trial was funded by Hvidovre University Hospital, though a minor contribution was received from a company fabricating orthoses. The company had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Furthermore the study result, whether positive or negative, did not have substantial implication for the firm. The risk of bias due to the source of funding is therefore considered minimal.

It should also be considered if the lack of difference found between the intervention and control groups could be due to lack of compliance. We intended to register the extent to which the allocated regimens were followed by implantation of pressure sensors in the orthoses. The sensors were custom made to measure the number of steps taken. Unfortunately the pressure sensors broke during treatment and we were not able to measure the difference in weight-bearing between groups. Patients and health personnel were not informed about the malfunction of the pressure sensors. A degree of sham-effect is therefore expected.

The large variation of data in study III makes one consider if the setup was imprecise. If seating of subjects in the isokinetic dynamometer lead to unrecognized bias or the isokinetic dynamometer functioned probably. However, the isokinetic dynamometer was used according to standard instructions and other studies performed on the same machine in the same period of time did not lead to excess spread of data. We therefore conclude that the spread of data is caused by an actual diversity in study population.

7.4 Study IV: A Novel Ultrasound Measurement of Achilles tendon Length and Elongation

The aim of study IV was to develop and validate a novel UL measurement. For that an observational, prospective, cross-sectional study design was used. We consider the study population to be static and data to be collected at a prolonged point in time. One can discuss the optimal time interval between test and re-test. The interval should be long enough for the investigators to forget their previous measurement but at the same time sufficiently short for the study subject to remain static. We decided for an interval between tests of three weeks, as we expected the length of an uninjured Achilles tendon to remain constant over time.

When designing an observational study one would like the study population to reflect the background population in order to be able to generalize the results. The size of the study population in paper IV taken into consideration a kind of selection bias must be expected. All the investigated persons were health personal, aged 26 to 63 years, without prior Achilles tendon problems who volunteered to participate. They probably differ from the background population in a range of unrecognized ways, but it is of less importance in the chosen setup where the left and the right sides were compared.

The next source of possible bias was the study setup. Positioning of the study subjects and execution of the measurements were done according to a written study protocol and agreed upon by the investigators just before measurement. Still some kind of bias must be expected as the measurement was personalized by the investigators and a learning curve effect is possible. Study subjects rotated between investigators positioned in the same room using three different US-scanners. Though no communication concerning the measurements was allowed between investigators they might have influenced each other. Finally, the measurement required visible marks to be made on the leg with a marker. The marks were removed between tests, but in some cases a vague mark persisted which might have influence the measurement of the following investigators.

It is difficult to control for the bias connected to the study setup. However, the risk of bias could possibly have been reduced study subjects had been positioned by the same person for all investigators. The risk of learning curve could have been reduced by a thorough training in the

measurement before the study period. Finally the same scanner could have been used by all three investigators and scans could have been done in isolated rooms with time enough between scans to allow for proper removal of the marks.

8 Summary of results

Experience is that marvelous thing that enables you
to recognize a mistake when you make it again.
Franklin Jones

8.1 Study I: Treatment of acute Achilles tendon rupture in Scandinavia

The questionnaire was returned by 138 of 148 departments (response rate: 93%). In Norway 73% of departments recommend operative treatment to all patients. This is significantly different from the remaining Scandinavian countries ($P < 0.001$) where only 9 – 18% recommends surgery to principally all patients. Some 92% of departments in Norway, 83% in Denmark and 65% in Sweden recommend surgical treatment for active people under the age of 60; this is only the case in 30% of departments in Finland ($P < 0.001$). Controlled early motion was used significantly less in Denmark 22% (5/23), Norway 38% (17/45) and Sweden 28% (11/40) compared to Finland 58% (15/26) ($P=0.015$). Two weeks after surgery 57% – 92% of departments across Scandinavia allow partial or full weight-bearing and it increases to 82% - 100% after 4 weeks. There is a significant difference between countries in educational level of performing surgeons. In Sweden 73% of departments answered that surgery was performed by a specialist in orthopedic surgery in the vast majority of cases. This is significantly different ($p = 0.001$) from Denmark (22%), Norway (19%) and Finland (41%).

8.2 Study II: The influence of early weight-bearing on clinical outcome

Thirty patients were randomized to each group; 29 and 27, respectively, were analyzed. There were no statistically significant differences between the weight-bearing and the non-weight-bearing groups at 12 months, except from a better health-related quality of life in the weight-bearing group ($p=0.009$). Mean ATRS at 12 months was 73 weight-bearing and 74 non-weight-bearing ($p=0.81$). The Heel-rise-work-test showed a total work performed of the injured limb compared to the uninjured limb of 53% weight-bearing and 58% non-weight-bearing ($p=0.37$) at 12 months. There were three re-ruptures in the weight-bearing group and two re-ruptures in the

non-weight-bearing (p=1.0). The weight-bearing group returned to work averagely six days earlier and resumed sport 38 days earlier compared to the non-weight-bearing group, this was not statistically significant.

8.3 Study III: The influence of early weight-bearing on biomechanical outcome

Thirty patients were randomized to each group; 26 and 20, respectively, were analyzed. There were no significant differences between the weight-bearing and the non-weight-bearing groups. Compared to the unaffected limb, peak passive torque was significantly lower for the affected limb at six months (91%, p=0.01), but not at 12 months (98%, p=0.51). Stiffness was significantly lower for the affected limb during the early part of dorsiflexion at six months (67%, p<0.001), and remained inferior at 12 months (77%, p<0.001). Irrespectively of group, a statistically significant decrease in the ability to store energy was seen in the affected limbs at both six (74%, p<0.001) and 12 months (82% p<0.001) follow up. Likewise, a statistically significant increase in torque relaxation was found in the affected limbs at both six (114%, p<0.001) and 12 months (111% p<0.001) follow up. The strength was significantly lower in the affected compared to the unaffected limb at both six (82%, p<0.001) and 12 months (93%, p=0.009).
As a surrogate for tendon elongation we looked at strength throughout range of motion. If tendon elongation was present one would expect strength to decline in the end of plantar flexion. As seen from figure 20 no difference between groups were found.

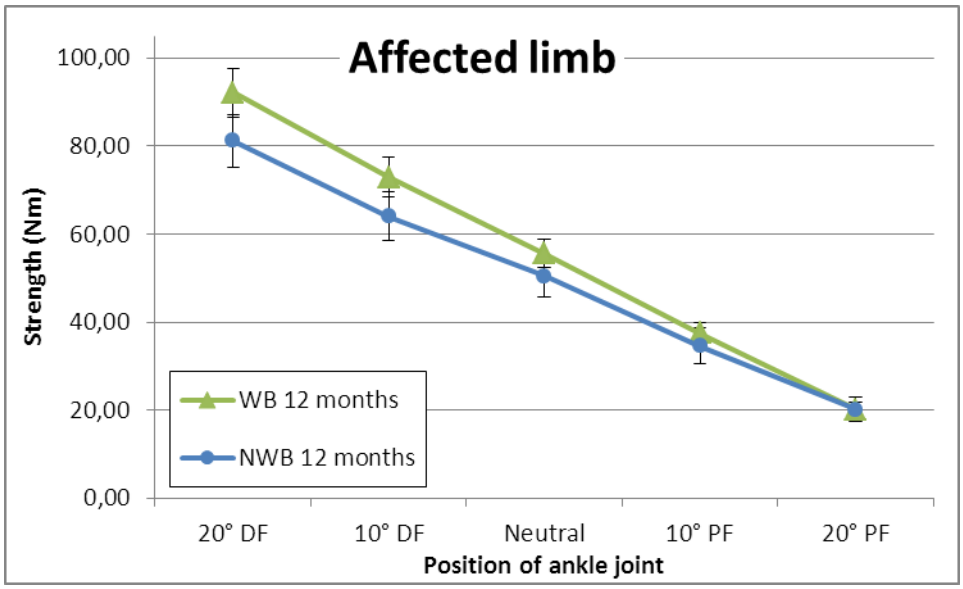

***Figure 20**: Strength throughout range of motion in the affected leg of the weight-bearing (WB) group and the non-weight-bearing (NWB) group.*

8.4 Study IV: A Novel Ultrasound Measurement of Achilles tendon Length and Elongation

The intra-rater evaluation of the novel US measurement showed excellent reliability (ICC 0.96) and an acceptable agreement (SEM 3.7mm and MDC 10.3mm). The inter-rater evaluation showed a systematic difference between US observers of 2.1mm – 4.5mm (p=0.001-0.036); reliability was excellent (ICC 0.97) and agreement acceptable (SEM 3.3mm and MDC 9.3mm). Validity was evaluated by comparison with MRI measurements. UL measurements were on average 3.8mm longer than US (p=0.001); the measurement error was 2%. No statistically significant difference in length was found between the left and the right Achilles tendon. However, a rather large spread of data was found; agreement SEM 4.1mm and MDC 11.5mm.

9 Discussion

All who drink of this treatment recover in a short time, except those whom it does not help, who all die. It is obvious, therefore, that it fails only in incurable cases.

Galen

The aim of this PhD thesis was to evaluate non-operative treatment of acute Achilles tendon rupture, addressing the question: 'What is the optimal non-operative treatment protocol for acute Achilles tendon rupture?'

Through the four papers of this thesis we have investigated 1) the status of treatment across Scandinavia and if departments adhere to the latest evidence, 2) the influence of immediate weight-bearing on patient reported and functional outcome, 3) the influence of immediate weight-bearing on biomechanical properties of the plantar flexor muscle-tendon complex, and 4) the validity and reliability of a novel ultrasound measurement of Achilles tendon Length and Elongation.

9.1 Treatment of acute Achilles tendon rupture in Scandinavia

9.1.1 Operative vs. non-operative treatment

There is increasing evidence supporting non-operative treatment as a safe and recommendable treatment for acute Achilles tendon rupture (chapter 3.1)[55,87,132,141]. The meta-analyses reveal convincing evidence that non-operative treatment yields a 2-3 times increased risk of re-rupture and a 4-5 times decreased risk of other complications[48,49,57,117,139]. Looking at functional results no clinical relevant differences are found in the meta-analyses[48,49,57,117,139]. The few studies that have assessed the patient perception through a PROM have not found any differences either[55,87].

However, no evidence of difference is not equivalent with evidence of no difference. All studies performed so far have been superiority studies, and as such they are not able to claim non-inferiority of a given treatment. Furthermore, one could argue that the trials lack ability to show the actual differences between operative and non-operative treatment due to imprecise outcome

parameters. Also it could be argued that the actual differences between treatment protocols are hidden in the heterogenic study populations. It is likely that a subgroup of the study populations would benefit from operative treatment and another subgroup from non-operative treatment. Dynamic ultrasound and Amlangs ultrasound classification have been suggested for use as selection tools to divide patients in subgroups, but no assessment of the measurements ability to predict final outcome has been made[4,61].

Considering the present literature the decision to treat operatively or non-operatively relies on an assessment of the severity of complications, in particular re-rupture and deep infection. The only published assessment of severity of complications was performed by Pajala et al.[94] They concluded that the outcome after a simple re-rupture without infection was satisfactory, whereas the outcome after a deep infection often was devastating.

The severity of complications taken into consideration, our humble conclusion is that the literature favors non-operative treatment as the standard treatment for acute Achilles tendon rupture.

9.1.2 Departments in Scandinavia treat operatively

In Norway 3 out of 4 departments treat all patients operatively. In Denmark and Norway 9 out of 10 departments, in Sweden 7 out of 10 and in Finland 3 out of 10 departments use operative treatment as their standard protocol for active people under the age of 60. According to the literature, this puts patients in increased risk of complications without clear functional benefits[48,49,57,117,139] and as such does not adhere to the latest evidence.

9.1.3 Controlled early motion vs. immobilization

Controlled early motion has been investigated in a number of experimental trials[6,19,31] and a few RCT's[24,51,80] (chapter 3.2.1). Furthermore controlled early motion has been used as standard treatment protocol in a number of RCT's testing operative vs. non-operative treatment[55,78,87,92, 117,132, 141]. The trials have not found clear positive or negative effects of controlled early motion, but tend to favor the mobilizing regimen. Also, the arguments used in chapter 9.1.1 concerning precision of the used outcome parameters and heterogeneity of the study population are valid here.

9.1.4 Departments in Scandinavia use of controlled early motion to some extend

Controlled early motion is used in 20% – 60% of departments in Scandinavia; the least in Denmark and the most in Finland. One could argue that the spread use of controlled early motion is in accordance with the emerging evidence which might favor controlled early motion.

9.1.5 Controlled early weight-bearing vs. immobilization

Controlled early weight-bearing has been investigated in one RCT looking at operatively treated patients[121] and been part of the standard treatment protocol in a number of other trials[27,104] (chapter 3.2.2). The RCT found a positive impact on health related quality of life during treatment. No other effects were found. Also, the arguments used in chapter 9.1.1 concerning precision of the used outcome parameters and heterogeneity of the study population are valid here.

9.1.6 Departments in Scandinavia use controlled early weight-bearing

Partial or full weight-bearing after surgical and non-surgical treatment is allowed in the majority of departments across Scandinavia within the first 2 – 4 weeks. Considering the little evidence on the subject no conclusion can be drawn in regard to whether departments adhere to the latest evidence.

9.2 Controlled early weight-bearing

The role of weight-bearing is of fundamental importance as it influences not only the quality of treatment but also the patient's ability to take care of him/herself. This ability is an essential part of most health related quality of life scores[39,124,127] and as such, when using a PROM, it is expectable to find an improved quality of life during treatment in the weight-bearing group, as it was done by Suchak et al.[121]

The evidence concerning controlled early weight-bearing, as discussed in chapter 9.1.5-6, does not allow for proper conclusions; especially concerning non-operative treatment, where no RCT's have been performed. Anyway, controlled early weight-bearing is used as the standard treatment in the majority of hospitals across Scandinavia, probably due to the obvious advantages concerning the patient's ability to take care of him/herself and the patients improved quality of life. The wide-spread use of controlled early rehabilitation can to some extend be considered a rough test of

safety, as major complications most probably would have been recognized. However, the most probable complication associated with controlled early weight-bearing, namely tendon elongation, cannot be expected to be recognized outside a controlled clinical setup.

In this thesis we investigated the influence of immediate weight-bearing on patient reported and functional outcome in study II and on biomechanical properties of the plantar flexor muscle-tendon complex in study III. No differences were found between the weight-bearing and the non-weight-bearing groups except for the expected difference in quality of life.
Again it is important to emphasize that no evidence of difference is not equivalent with evidence of no difference. The trials were not designed as a non-inferiority trials and as such they cannot claim immediate- and non-weight-bearing to be equally effective in the treatment of acute Achilles tendon rupture. Also the arguments used in chapter 9.1.1 concerning precision of the used outcome parameters and heterogeneity of the study population are valid here.

9.3 Length-measurement

Elongation of the Achilles tendon after acute rupture is well known and associated with inferior clinical outcome[50,78,81,115]. Therefore, it is desirable to identify the group of patients in high risk of elongation in the acute or early phase after acute Achilles tendon rupture in order to individualize and thus optimize their treatment. A clinically applicable, accurate and easy to perform method for evaluating Achilles tendon length and elongation is needed for this purpose.

A range of length measures have been described in chapter 4.4[4,23,50,64,95,99,102,105,118,144], but they do not fulfill the above mentioned criteria. The aim of this study was to develop and validate a method which can determine Achilles tendon length and elongation accurately in a clinical setting using standard US equipment.

The first question that arises is whether it makes sense to investigate the length of a ruptured tendon. Does a ruptured tendon have a length or is it merely two flowing tendon ends. With the novel UL measurement we chose two anatomical landmarks at the periphery of the tendon. One could say that instead of investigating the tendon itself, we investigated if changes were made to the working length of the suralis muscle in relation to the calcaneal bone. When the tendon ruptures, the position of the proximal end of the Achilles tendon varies with knee flexion and

contraction of the Triceps surae muscle and the position of the distal end of the Achilles tendon varies with the position of the ankle joint[101,108]. It is therefore paramount for a measurement of the ruptured Achilles tendon to use a standardized position of the ankle and knee joint.

The validity of the measurement compared to MRI was acceptable (error 2%). The length assessment methods are different in US and MRI and as such a difference must be expected. MRI has not been validated for this specific length measure, thus it could be argued that our validity test is invalid. However, MRI was considered to be the best available non-invasive modality to use as gold standard concerning Achilles tendon length.

The reliability and agreement of the novel US measurement was comparable with the more advanced and logistically more demanding methods described in chapter 4.4[102,115]. For comparison between groups of non-injured subjects, differences of more than 4mm can be detected. For repeated assessment of individual subjects, differences of more than 10mm can be detected. If the findings by Silbernagel et al.[115,125] of an average elongation after ATR of 2.5-3.5cm holds to be true, the precision of the novel US measurement is fully acceptable.

Finally, the large variation in length between the right and the left side in healthy people introduces an error in all measurements using the healthy leg as reference. We do not see an alternative reference value, but it is important for clinicians and researchers to be aware of this additional error.

10 Conclusion

Life is the art of drawing sufficient conclusions from insufficient premises.

Samuel Butler

Non-operative treatment using controlled early weight-bearing after acute Achilles tendon rupture is safe. It may be the standard of care in national and international treatment guidelines concerning acute Achilles tendon rupture.

10.1 Treatment does not adhere to evidence based guidelines.

Operative treatment and controlled early weight-bearing is the preferred treatment protocol for acute Achilles tendon rupture in Scandinavia. This is in contrast with the latest evidence, which may favor non-operative treatment as the standard treatment for acute Achilles tendon rupture.

10.2 Controlled early weight-bearing is safe

It seems reasonable to recommend immediate weight bearing in a non-operative, dynamic treatment protocol as a safe treatment modality for acute Achilles tendon rupture. Immediate weight-bearing improves health related quality of life during treatment and does not seem to have detrimental effect on patient reported and functional outcome and on biomechanical properties of the plantar flexor muscle-tendon complex.

10.3 The novel UL measurement is valid and reliable

The novel US measurement showed good validity, reliability and agreement. For comparison between groups of non-injured subjects differences of more than 4mm can be detected. For repeated assessment of individual subjects differences of more than 10mm can be detected. A measurement error of 2% was found. No systematic difference in length of the right and left Achilles tendon was found, but a rather large variation. Due to this an error of 5mm is introduced when looking at groups of patients using the uninjured side as reference and an error of 13mm for repeated assessment of individual subjects.

11 Perspective and future research

'The more you know, the more you realize you know nothing.'

Socrates

The best treatment of acute Achilles tendon rupture has been discussed for a century. This thesis is a small step on the road of evidence.

An unacceptable diversity of treatment protocols is seen in Scandinavia. Future research should aim at developing a uniform treatment algorithm.

RCT's have focused on operative vs. non-operative treatment. There is a need for better investigation of the influence of rehabilitation. Future trials should investigate the area of controlled early motion and the combination of controlled early motion and weight-bearing.

An unacceptable fraction of patients acquiring an acute Achilles tendon rupture do not return to their premorbid level of function. We do not know why and we are not able to predict who will re-rupture and who will heal in elongation. If this subgroup could be identified in the acute phase of rupture or early phase of treatment, e.g. by US measurements, we might be able to individualize and improve their treatment. Future research should focus on identifying measures to identify this subgroup.

The novel US measurement should be tested in a population with Achilles tendon rupture and it should be correlated to final outcome. The same should be done for other US measurements like Amlangs US classification system[4].

All RCT's published to date have considered patients the same and used re-rupture as the primary outcome. Future research could stratify people according to their risk profiles and use validated outcome measures.

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13 Annex

Annex A

Livskvalitet

Følgende spørgsmål omhandler i hvor stor udstrækning patienten har følt sig begrænset på grund af behandlingen som et gennemsnit over de sidste 8 uger.

1. Var du begrænset i dine hverdagsaktiviteter (eks.: indkøb, madlavning, toilet besøg) som følge af støvlebehandlingen?

Meget begrænset												Slet ikke begrænset
	0	1	2	3	4	5	6	7	8	9	10	

2. Var du begrænset i dit arbejde (i forhold til dine funktioner før du kom til skade) som følge af støvlebehandlingen?

Meget begrænset												Slet ikke begrænset
	0	1	2	3	4	5	6	7	8	9	10	

3. Var du begrænset i dit sociale liv (eks.: Biograf tur, samvær med venner, parforhold) som følge af støvlebehandlingen?

Meget begrænset												Slet ikke begrænset
	0	1	2	3	4	5	6	7	8	9	10	

4. Var dit humør påvirket som følge af støvlebehandlingen?

Meget påvirket												Slet ikke påvirket
	0	1	2	3	4	5	6	7	8	9	10	

5. Hvad var dit gennemsnitlige smerteniveau?

Meget påvirket												Slet ikke påvirket
	0	1	2	3	4	5	6	7	8	9	10	

Annex B

Spørgeskema omhandlende behandling af akut achillesseneruptur i Danmark

Vi vil bede dig bruge 5 minutter på at udfylde vedlagte korte spørgeskema.

Vi ønsker at klarlægge, hvad der er den foretrukne behandling af akut achillesseneruptur på landets ortopædkirurgiske afdelinger.

Eventuelle spørgsmål kan rettes til Kristoffer Barfod:
Tlf. 61 300 288.
E-mail: kbarfod@dadlnet.dk

Spørgeskemaet bedes returneret inden 2 uger til:
Kristoffer Barfod
Ortopædkirurgisk ambulatorium, afsn. 333
Hvidovre Hospital
Kettegård Alle 30
2650 Hvidovre

Med venlig hilsen

Læge, PHD-studerende Kristoffer Barfod,
Ortopædkirurgisk afdeling, Hvidovre Hospital

Læge, PHD-studerende Anders Boesen
Institut for idrætsmedicin, Bispebjerg Hospital

Generelt

Hospital / enhed _____

	Ja	Nej
Behandles akut achillesseneruptur på din afdeling?	☐	☐

Hvordan fastlægges diagnosen akut achillesseneruptur?

- ☐ Diagnosen stilles klinisk, kun i sjældne tilfælde anvendes billeddiagnostik
- ☐ Billeddiagnostik anvendes i de fleste tilfælde for at sikre diagnosen
- ☐ Andet: _____
  _____

Hvordan besluttes valg af behandling?

- ☐ Det er en individuel vurdering foretaget af behandlende læge i samarbejde med patienten.
- ☐ Der er klare kriterier for hvem der skal behandles operativt og hvem der skal behandles konservativt, men der er fortsat rum til individuel vurdering.
- ☐ Der er klare kriterier for hvem der skal behandles operativt og hvem der skal behandles konservativt, der lades meget ringe rum til individuel vurdering.
- ☐ Andet: _____
  _____

Har afdelingen en nedskreven instruks vedrørende behandling af ASR:

- ☐ Afdelingen har en gyldig nedskreven instruks der følges i langt de fleste tilfælde.
- ☐ Afdelingen har en instruks, men den følges kun delvist, og der er rum for individuelle vurderinger blandt afdelingens læger.
- ☐ Afdelingen har ikke en gyldig nedskreven instruks.
- ☐ Andet: _____
  _____

Hvordan inddrages patienten i behandlingsvalget:

- ☐ Vi lægger vægt på at patienten selv skal træffe beslutning omkring behandlingsvalg
- ☐ Afdelingen har en klar anbefaling omkring behandlingsvalg, men patientens ønske har afgørende betydning.
- ☐ Afdelingen er af den overbevisning at behandlingsvalget skal forestages af lægen og ikke overlades til patienten, forudsat at patiens rettigheder overholdes.
- ☐ Andet: _____

Operativ behandling

Hvem anbefales operativ behandling?

- [ ] Vi anbefaler operativ behandling til stort set alle
- [ ] Vi anbefaler operativt behandling til raske mennesker med højt aktivitetsniveau og en alder under 60 år
- [ ] Vi anbefaler stort set kun operativ behandling til aktive idrætsfolk og andre med særdeles høje krav til achillessenens funktion
- [ ] Vi anbefaler kun operativ behandling ved oversete rupturer, hvis patienten er behandlet med binyrebarkhormon eller ved skarp læsion, samt evt. i ganske få andre tilfælde
- [ ] Andet: _____
  _____

Hvilke af følgende forhold vurderer du mest korrekt?

- [ ] Vi behandler mere end 90% af alle akutte achillessenerupturer operativt
- [ ] Vi behandler 50% - 90% af alle akutte achillessenerupturer operativt
- [ ] Vi behandler 10% - 50% af alle akutte achillessenerupturer operativt
- [ ] Vi behandler mindre end 10% af alle akutte achillessenerupturer operativt

Hvilken operationsteknik anvendes som første valg?

- [ ] Åben operation med end-to-end sutur ad modum Krackow, modificeret Kessler eller Bunnel.
- [ ] Forstærket end-to-end sutur hvor plantarissenen anvendes til at forstærke den reparerede sene.
- [ ] Minimalt invasiv end-to-end sutur
- [ ] Der er ikke en fast anbefaling, det er op til den enkelte kirurg at vælge operationsteknik
- [ ] Anden teknik: _____
  _____

Hvem udfører operationerne?

- ☐ Operationerne udføres i langt de fleste tilfælde af speciallæger tilknyttet fod-ankel sektor eller traumatologisk sektor
- ☐ Operationerne udføres i langt de fleste tilfælde af speciallæger
- ☐ Operationerne udføres af speciallæger, kursister eller introlæger
- ☐ Andet: _____
  _____

Hvilken postoperativ bandagering anvendes?

- ☐ Gips eller walker bandage i 6-8 uger med gradvis opretning af fodledet. Der er ikke mulighed for at bevæge over ankelledet.
- ☐ Gips eller walker bandage i 6-8 uger med gradvis opretning af fodledet. Efter ca. 2 uger dynamiseres over ankelledet ved at patienten flere gange dagligt tager foden ud af støvlen og bevæger ankelledet igennem.
- ☐ Gips bandage de første uger efterfulgt af behandling i orthose med bevægelighed over ankelledet.
- ☐ Der er ikke en fast anbefaling, det er op til den enkelte kirurg at vælge Postoperativt regime.
- ☐ Andet: _____
  _____

Hvornår må der belastes på benet (sæt gerne et kryds i hver kolonne)?

Delvis	Fuld	
☐	☐	Med det samme når bandagen er anlagt
☐	☐	Efter 2 uger
☐	☐	Efter 4 uger
☐	☐	Efter 6 uger
☐	☐	Efter 8 uger

- ☐ Andet: _____
  _____

Hvor ofte kontroleres patienten af en læge?

- ☐ Patienten kontroleres af læge 1 gang (F.eks. ved suturfjernelse)
- ☐ Patienten kontroleres af læge 2 gange (F.eks.ved suturfjernelse og afbandagering)
- ☐ Patienten kontroleres af læge 3 eller flere gange
- ☐ Andet: _____
  _____

Konservativ behandling

Hvilken bandagering anvendes?

- ☐ Gips eller walker bandage i 6-8 uger med gradvis opretning af fodledet. Der er ikke mulighed for at bevæge over ankelledet.
- ☐ Gips eller walker bandage i 6-8 uger med gradvis opretning af fodledet. Efter ca. 2 uger dynamiseres over ankelledet ved at patienten flere gange dagligt tager foden ud af støvlen og bevæger ankelledet igennem.
- ☐ Gips bandage de første uger efterfulgt af behandling i skinne med bevægelighed over ankelledet.
- ☐ Der er ikke en fast anbefaling, det er op til den enkelte læge at vælge konservativt regime.
- ☐ Andet: _____
  _____

Hvornår må der belastes på benet (sæt gerne et kryds i hver kolonne)?

Delvis	Fuld	
☐	☐	Med det samme når bandagen er anlagt
☐	☐	Efter 2 uger
☐	☐	Efter 4 uger
☐	☐	Efter 6 uger
☐	☐	Efter 8 uger

- ☐ Andet: _____
  _____

Hvor ofte kontroleres patienten af en læge?

- ☐ Patienten kontroleres af læge 1 gang (F.eks. ved afbandagering)
- ☐ Patienten kontroleres af læge 2 gange (F.eks.ved kilefjernelse og afbandagering)
- ☐ Patienten kontroleres af læge 3 eller flere gange
- ☐ Andet: _____
  _____

Kasuistikker

Hvordan behandles følgende patienter med akut achillesseneruptur på din afdeling?

Patient nr 1: 32 årig mand, ASA 1, tidligere professionel bordtennisspiller, idrætslærer og træner for landsholdet i bordtennis, ingen sukkersyge, ikke ryger, ingen tidligere sygdom i achillessenen.

☐ Konservativ behandling ☐ Operativ behandling

Patient nr 2: 52 årig mand, ASA 1, veltrænet, ingen sukkersyge, politimand, Ikke ryger, har gennem det sidste ½ år haft irritation og smerter fra achillessenen og inden for den sidste måned fået 2 injektioner steroid omkring senen.

☐ Konservativ bahandling ☐ Operativ behandling

Patient nr 3: 65 årig mand, ASA 2, udseende yngre end alder, ingen sukkersyge, aktiv med cykling, tidligere ryger, ingen tidligere sygdom i achillessenen.

☐ Konservativ behandling ☐ Operativ behandling

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Treatment of Acute Achilles Tendon Rupture in Scandinavia Does Not Adhere to Evidence-based Guidelines: A Cross-sectional Questionnaire-based Study of 138 Departments

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ABSTRACT

The best treatment of acute Achilles tendon rupture has been discussed for decades. During the past half decade, evidence has increased in favor of nonoperative treatment and dynamic and weightbearing rehabilitation. We hypothesized that the treatment strategies would show great variation and that adherence to evidence-based recommendations would not be as good as desired. The purpose of the present study was to investigate how acute Achilles tendon rupture is treated in Scandinavia. A questionnaire was distributed to all orthopedic departments treating acute Achilles tendon ruptures in Denmark, Sweden, Norway, and Finland. The questionnaire was returned by 138 of 148 departments (response rate 93%). Two-way tables with Fisher's exact test were used for statistical analysis. In Denmark, Norway, Sweden, and Finland, 19 of 23 (83%), 44 of 48 (92%), 26 of 40 (65%), and 8 of 27 (30%) departments recommended surgical treatment ($p < .001$). Dynamic rehabilitation was used significantly less often in Denmark (5 of 23 [22%]), Norway (17 of 45 [38%]), and Sweden (11 of 40 [28%]) than in Finland (15 of 26 [58%]; $p = .015$). A significant difference was found among the countries in the educational level of the performing surgeons ($p < .001$). Surgical treatment was the treatment of choice in Danish, Norwegian, and Swedish hospitals regardless of the increasing evidence favoring nonoperative treatment. Although increasing evidence has favored dynamic rehabilitation, it has gained limited use across Scandinavia. Weightbearing was used in most hospitals. Surgery was performed by junior surgeons in most hospitals across Scandinavia. Treatment algorithms showed considerable variation and often did not adhere to the clinical evidence.

Acute Achilles tendon rupture is a common injury, with an incidence of 11 to 37/100,000 (1–3). The best treatment method has been the subject of ongoing debate for decades. Acute Achilles tendon rupture can be treated surgically or nonsurgically. Rehabilitation can be dynamic or immobilizing and can be weightbearing or non-weightbearing.

In the 1980s and 1990s, a number of randomized controlled trials, comparing surgical and nonsurgical treatment, suggested better outcomes after surgery owing to the higher rate of rerupture in the nonsurgical group (4–6). Other reports have been unable to show significant benefits with surgical treatment (7–14). In 2012, 3 high-quality meta-analyses (15–17) comparing surgical and nonsurgical treatment of Achilles tendon ruptures all found a significantly higher rerupture rate but a significantly lower overall complication rate in the nonsurgically treated patients. However, in these studies, no distinction was made between studies using a dynamic rehabilitation protocol and those using immobilization. No significant differences in functional outcomes were found between the 2 treatment methods.

In 2007, Twaddle and Poon (10) drew attention to dynamic rehabilitation, suggesting that controlled early motion was the most important part of treatment of ruptured Achilles tendons.

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Table 1
Response rate

Country	Response Rate (%)
Denmark	100 (23/23)
Sweden	89 (40/45)
Norway	96 (48/50)
Finland	90 (27/30)
Sum	93 (138/148)

Subsequent to this observation, 3 randomized controlled trials comparing dynamic treatment protocols in surgically and nonsurgically treated patients did not show statistically significant differences in the rerupture rates (10–12). This observation was confirmed by a recent meta-analysis. When considering the subgroup of studies using dynamic rehabilitation, they did not find any difference in the rerupture rate between surgical and nonsurgical treatment (16,17).

Weightbearing during rehabilitation of Achilles tendon ruptures has been shown to have a positive effect on the health-related quality of life, and it might allow for a quicker return to work (18). It has been shown in experimental rodent models that the increased strain of weightbearing on the tendon is beneficial for healing (19). In humans, Suchak et al (18) found no detrimental effects from weightbearing from the second postoperative week in surgically treated patients.

Given the historical diversity of the published results and recommendations, it could be anticipated that the treatment of Achilles tendon ruptures would differ widely among departments treating this injury. It is doubtful whether all departments treating Achilles tendon ruptures adhere to the latest evidence. We, therefore, performed a survey of Scandinavian centers to investigate the use of surgical treatment, dynamic rehabilitation, and weightbearing.

Patients and Methods

The present study was conducted as a questionnaire-based, cross-sectional study investigating the use of surgical treatment, dynamic rehabilitation, and weightbearing. All orthopedic departments treating acute Achilles tendon ruptures in Denmark, Sweden, Norway, and Finland were identified. Only public hospitals were included, because private hospitals, in our experience, have played a negligible role in the treatment of acute Achilles tendon rupture in Scandinavia. The questionnaire was sent to the physician responsible for Achilles tendon treatment when possible and, otherwise, to the head of the department. If the physician did not respond, a reminder was sent by electronic mail, regular mail, or telephone. Data were collected from October 2011 to October 2012.

The questionnaire was developed in Danish and translated by bilingual speakers into Swedish, Norwegian, and Finish. No formal validation of the translations was performed. The questionnaire consisted of 17 questions. The questions were multiple choice, with 4 to 6 possible answers, including the possibility of a free text answer. The questionnaire was divided into 4 parts. Part 1 investigated Achilles tendon rupture diagnostics, including how the choice of treatment was made and to what degree the patient was involved in the decision-making process (4 questions). Part 2 investigated which patients were recommended for surgical treatment, which surgical technique was used, and what type of postoperative regimen was offered (7 questions). Part 3 investigated what type of nonsurgical treatment was offered (3 questions). Dynamic rehabilitation was defined as a rehabilitation protocol allowing movement of the ankle after week 2. Part 4 consisted of 3 patient cases in which the preference for surgical or nonsurgical treatment had to be determined.

A paper version and an electronic version of the questionnaire were developed. For those physicians with email, the electronic questionnaire was used; otherwise, the paper version was used. In Sweden and Finland, all data were collected electronically. In Denmark, 7 hospitals answered electronically, and 16 used the paper version. In Norway, all data were collected using the paper version. The questionnaire was returned by 138 of 148 departments (93%; Table 1).

The investigational team participated in the development and translation of the questionnaire and the collection of data. The statistical analysis was performed by 2 of us (K.W.B., A.T.). Statistical analysis was performed using the Statistical Package for Social Sciences, version 12.0, for Windows (SPSS, Chicago, IL). Two-way tables with Fisher's exact test were used.

Results

Use of Surgical Treatment

In Norway, 73% of the departments recommended surgery to all patients. This percentage was significantly different from the remaining Scandinavian countries ($p < .001$), in which only 9% to 18% recommended surgery principally to all patients. About 92% of the departments in Norway, 83% in Denmark, and 65% in Sweden recommended surgical treatment for active people younger than 60 years old. This was the case in only 30% of departments in Finland ($p < .001$). Considering the surgical treatment of active sportsmen, we found the same trend: 100% of departments in Norway, 91% in Denmark, and 85% in Sweden recommended surgery, but only 74% of departments in Finland recommended surgery ($p = .001$; Table 2). The same numbers were reflected in the patient cases (see Table 7).

Use of Dynamic Rehabilitation

After surgery, dynamic rehabilitation was used in 35% of the departments in Denmark compared with 50% in Sweden, 52% in Norway, and 64% in Finland ($p = .20$). When treating nonsurgically, dynamic rehabilitation was used in 22% of the departments in Denmark, 28% in Sweden, and 38% in Norway compared with 58% in Finland ($p = .015$; Table 3).

Use of Weightbearing

Partial or full weightbearing 1 day after surgery was allowed in 26% of the departments in Finland and 30% in Denmark compared with 42% in Norway and 62% in Sweden ($p = .018$). At 2 weeks after surgery, 57% to 92% of departments allowed partial or full

Table 2
Use of surgical treatment

Response	Denmark	Sweden	Norway	Finland	*p* Value*
1. In principle, all patients are recommended surgery	9 (2/23)	18 (7/40)	73 (35/48)	11 (3/27)	<.001
2. Healthy and active people <60 years are recommended surgery	83 (19/23)	65 (26/40)	92 (44/48)	30 (8/27)	<.001
3. Active sportsmen and those with excessive demands to their Achilles tendons are recommended surgery	91 (21/23)	85 (34/40)	100 (48/48)	74 (20/27)	.001
4. Only patients with a delayed diagnosis, treated with corticosteroids, sharp lesions, and a few other cases are recommended surgery	9 (2/23)	15 (6/40)	0 (0/48)	26 (7/27)	.001

Data presented as percentages, with numbers in parentheses.
The departments were asked which patients they would recommend to undergo surgery; responses 1, 2, and 3 are summative; that is, those who would recommend surgery for all patients (response 1) also would recommend surgery for healthy and active people (response 2), and so forth.
* Difference between countries.

Table 3
Use of dynamic rehabilitation

Country	Dynamic Rehabilitation	
	Used after Surgery	Used with Nonoperative Treatment
Denmark	35 (8/23)	22 (5/23)
Sweden	50 (20/40)	28 (11/40)
Norway	52 (25/48)	38 (17/45)
Finland	64 (22/39)	58 (15/26)
p value	.20	.015

*Difference between countries.

weightbearing across Scandinavia, with the percentage increasing to 82% to 100% after 4 weeks.

Full weightbearing 1 day after surgery was allowed in 0% of the departments in Finland and 10% in Norway compared with 26% in Denmark and 31% in Sweden ($p = .001$). At 2 weeks after surgery, 22% of the departments in Finland allowed full weightbearing compared with 44% in Norway, 48% in Denmark, and 64% in Sweden ($p = .009$; Table 4).

The same trend was seen after nonoperative treatment. However, the departments across Scandinavia were slightly more restrictive in allowing weightbearing after nonoperative treatment (Table 5).

Surgeons' Experience Level

In Sweden, 73% of the departments responded that surgery was performed by a specialist in orthopedic surgery in the vast majority of cases. This was significantly different ($p = .001$) from the proportion in Denmark (22%), Norway (19%), and Finland (41%; Table 6).

Patient Cases

Case 1 concerned a 32-year-old, nonsmoking athlete with no comorbidities. This patient would have been recommended surgical treatment in 91% of the departments in Denmark, 85% in Sweden, and 100% in Norway. The difference from that in Finland (70%) was statistically significant ($p < .001$; Table 7).

Case 2 concerned a 52-year-old, nonsmoking, and physically fit male. He had experienced tendinosis of the Achilles tendon during the previous 6 months and had undergone 2 injections with corticosteroids within the previous month. This patient would have been recommended surgical treatment in 61% of the departments in Denmark, 73% in Sweden, and 94% in Norway. The difference from that in Finland (48%) was statistically significant ($p < .001$; Table 7).

Case 3 concerned a 65-year-old male with minor comorbidities (American Society of Anesthesiologists class 2), no diabetes, and no former problems with his Achilles tendon. This patient would have been recommended surgical treatment in 52% of the departments in Denmark, 45% in Sweden, and 87% in Norway. Again, the difference from that in Finland (26%) was statistically significant ($p < .001$; Table 7).

Discussion

Strong evidence supports nonoperative treatment and dynamic rehabilitation as a safe and recommendable treatment of choice for acute Achilles tendon ruptures. Furthermore, weightbearing seems safe and beneficial after surgery. The purpose of the present study was to investigate whether the treatment of acute Achilles tendon rupture in Scandinavia adheres to evidence-based recommendations.

Use of Surgical Treatment

The results of the present study have shown a remarkable variation of treatment across Scandinavia. The choice of treatment varied from hospital to hospital within cities or countries and between countries. In Denmark, Sweden, and Norway, most departments recommended surgical treatment, but in Finland, most departments recommended nonoperative treatment.

In Norway, most departments recommended surgical treatment to practically all patients. The decision was independent of patient age, activity level, and etiology of the lesion. In Denmark and Sweden, the main criteria for surgery was age younger than 60 years and an active lifestyle. This differed from Finland, in which excessive demands to the tendon and the etiology of the rupture were the main criteria for surgery.

No evidence has been presented in published studies concerning which patients should undergo surgery. The reports advocating surgical treatment have claimed faster recovery, better strength, and a lower rerupture rate (5,16). Advocates for nonoperative treatment have claimed less disabling complications, the same functional result, and the same low rerupture rate (15–17). Meta-analyses considering all studies comparing surgical and nonsurgical treatment have found a lower rerupture rate and, potentially, marginally better functional outcomes in the surgical group. However, when stratifying the data and considering only those studies using a modern dynamic rehabilitation protocol, the rerupture rate and functional results did not differ between the 2 treatments (16,17). In summery, the complication rate associated with surgery is significantly increased compared with that associated with nonoperative treatment, and, when using a modern rehabilitation protocol, no important differences in the repeat rupture rate or functional results

Table 4
Use of weightbearing after surgery stratified by interval until weightbearing allowed

Week	Denmark		Sweden		Norway		Finland		*p* Value*	
	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full
0	30 (7/23)	26 (6/23)	62 (24/39)	31 (12/39)	42 (20/48)	10 (5/48)	26 (7/27)	0 (0/27)	.018	.001
2	57 (13/23)	48 (11/23)	92 (36/39)	64 (25/39)	77 (37/48)	44 (21/48)	74 (20/27)	22 (2/27)	.012	.009
4	82 (19/23)	61 (14/23)	97 (38/39)	82 (32/39)	85 (41/48)	56 (27/48)	100 (27/27)	56 (15/27)	.024	.042
6	100 (23/23)	91 (21/23)	100 (39/39)	95 (37/39)	94 (45/48)	73 (35/48)	100 (27/27)	96 (26/27)	.28	.007
8	100 (23/23)	100 (23/23)	100 (39/39)	100 (39/39)	94 (45/48)	98 (47/88)	100 (27/27)	100 (27/27)	.28	1.00
Other	0 (0/23)	0 (0/23)	0 (0/39)	0 (0/39)	6 (3/48)	2 (1/48)	0 (0/27)	0 (0/27)	.28	1.00

Data presented as percentages, with numbers in parentheses.
The answers are summative: those allowing weightbearing 1 day postoperatively also allowed weightbearing after 2 weeks, and so forth.
* Difference between countries.

Table 5
Use of weightbearing when treating nonoperatively stratified by interval until weightbearing allowed

Week	Denmark		Sweden		Norway		Finland		*p* Value*	
	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full	Partial or Full	Full
0	23 (5/22)	18 (4/22)	58 (23/40)	28 (11/40)	33 (13/39)	13 (5/39)	15 (4/27)	0 (0/27)	.002	.010
2	46 (10/22)	46 (10/22)	73 (29/40)	50 (20/40)	49 (19/39)	31 (12/39)	44 (12/27)	15 (4/27)	.053	.016
4	64 (14/22)	59 (13/22)	85 (34/40)	70 (28/40)	64 (25/39)	41 (16/39)	89 (24/27)	33 (9/27)	.029	.010
6	96 (21/22)	77 (17/22)	93 (37/40)	83 (33/40)	82 (32/39)	54 (21/39)	100 (27/27)	86 (23/27)	.067	.013
8	96 (21/22)	96 (21/22)	100 (40/40)	100 (40/40)	95 (37/39)	100 (39/39)	100 (27/27)	100 (27/27)	.29	.17
Other	4 (1/22)	4 (1/22)	0 (0/40)	0 (0/40)	5 (2/39)	0 (0/39)	0 (0/27)	0 (0/27)	.29	.17

Data presented as percentages, with numbers in parentheses.
The answers are summative: those allowing weightbearing 1 day postoperatively also allowed weightbearing after 2 weeks, and so forth.
* Difference between countries.

have been shown. Therefore, it does not seem commendable to treat patients surgically by default.

Use of Dynamic Rehabilitation

Dynamic rehabilitation was used in 20% to 60% of departments in Scandinavia, with the least percentage in Denmark and the most in Finland. The published data support dynamic rehabilitation for healing flexor tendons (20,21); and animal studies have shown a reduced strength of immobilized Achilles tendons 3 times less than that of mobilized tendons (22). The use of dynamic rehabilitation has been supported by the latest randomized clinical trials comparing surgical and nonsurgical treatment (10–12) and the latest meta-analyses (16,17). Given the present published data, it seems dynamic rehabilitation protocols should be recommended after both surgical and nonoperative treatment. However, no randomized controlled trials have compared dynamic and immobilized rehabilitation protocols.

Use of Weightbearing

Partial or full weightbearing after surgical and nonoperative treatment was allowed in most departments across Scandinavia within the first 2 to 4 weeks. Sweden was the most aggressive concerning full weightbearing, and Finland was more restrictive. Across Scandinavia, the departments tended to be slightly more restrictive using nonoperative treatment than using surgery. The published data support full weightbearing from week 2 after surgery, although only 1 randomized controlled trial has investigated the use of weightbearing (18). No data are available from humans concerning weightbearing after nonoperative treatment. Rodent models have shown the beneficial effects of mechanical stimulation after nonoperative treatment of dissected Achilles tendons (19).

From the published data, it does seem safe to recommend early weightbearing after surgical treatment. However, additional knowledge concerning optimal loading of the healing tendon is necessary to determine the best protocol for weightbearing. High-quality, randomized controlled trials investigating weightbearing after nonoperative treatment are needed.

Table 6
Surgeons' experience level

Country	Surgery for Acute Achilles Tendon Rupture Mainly Performed by Orthopedic Surgical Specialists
Denmark	22 (5/23)
Sweden	73 (29/40)
Norway	19 (9/48)
Finland	41 (11/27)
p value	<.001

Data presented as percentages, with numbers in parentheses.

Surgeons' Experience Level

The results of the present study have shown that surgery of Achilles tendon ruptures is performed by a specialist in orthopedic surgery in 73% of the departments in Sweden, although this was the case in only 22% of departments in Denmark, 19% in Norway, and 41% in Finland. We expected the experience level of the surgeon to be an important factor of success, just as it has been in other fields of surgery (23,24). As such, one could expect the quality of surgery to be better in Sweden than in the rest of Scandinavia. However, it was beyond the scope of the present cross-sectional survey to draw conclusions concerning the surgeon skill level. National differences in healthcare systems and educational system should also be considered.

Study Limitations

The survey was designed to investigate the treatment of choice in orthopedic departments across Scandinavia and did not consider the size of these departments. Thus, the survey could not be used to answer quantitative questions concerning the number of patients receiving a given treatment. The degree of data completeness was good, with a reply rate of 93%. However, a risk of bias existed, because the remaining 7% might have included those with the least adherence to the evidence-based recommendations. Also, our definition of dynamic rehabilitation included the use of a hinged orthosis. This led to a risk of overestimating the true number of departments using a dynamic rehabilitation protocol because some might have used the hinged orthosis as a static orthosis. Finally, the translation of the questionnaire was not validated; therefore, a risk of data distortion among the countries was possible.

In conclusion, we found a remarkable variation of treatment across Scandinavia. In Finland, the treatment policies seemed closer to the evidence-based recommendations compared with the rest of Scandinavia. Surgical treatment was the treatment of choice in most Danish, Norwegian, and Swedish hospitals, regardless of increasing evidence favoring nonoperative treatment. Despite increasing evidence favoring dynamic rehabilitation, it has gained limited use across Scandinavia. Weightbearing was used in most hospitals in Scandinavia. Surgery was performed by junior surgeons in most hospitals across Scandinavia, warranting a focus on the supervision of surgery. The treatment algorithms in Scandinavia varied considerably and often did not adhere to evidence-based recommendations.

Table 7
Patient cases

Case	Denmark	Sweden	Norway	Finland	*p* Value
1. 32-year-old, nonsmoking athlete with no comorbidities	91 (21/23)	85 (34/40)	100 (47/47)	70 (19/27)	<.001
2. 52-year-old, nonsmoking, and physically fit male with tendonitis for 6 months, who had undergone 2 corticosteroid injections within previous month	61 (14/23)	73 (29/40)	94 (44/47)	48 (13/27)	<.001
3. 65-year-old male with light comorbidities (ASA class 2), no diabetes, and no former problems from Achilles tendon; an active cyclist	52 (12/23)	45 (18/40)	87 (40/46)	26 (7/27)	<.001

Abbreviation: ASA, American Society of Anesthesiologists.
Data presented as percentages, with numbers in parentheses.

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Non-operative, dynamic treatment of acute Achilles tendon rupture: The influence of early weight-bearing on clinical outcome. A blinded, randomized, controlled trial.

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Non-operative, dynamic treatment of acute Achilles tendon rupture: The influence of early weight-bearing on clinical outcome. A blinded, randomized, controlled trial.

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ABSTRACT

Background: Dynamic rehabilitation after non-operative treatment of acute Achilles tendon rupture (ATR) has been suggested to be an important part of treatment yielding functional outcome and re-rupture rates comparable to that of operatively treated ATR. However, the optimal non-operative treatment protocol remains to be clarified, particularly the role of weight-bearing (WB) during early rehabilitation.
The purpose of this study was to compare immediate WB with non-WB in a non-operative, dynamic treatment protocol for ATR.

Methods: The study was conducted as a blinded, randomized, controlled, parallel, superiority trial (RCT). Patients aged 18 to 60 years were eligible for inclusion. Both groups were treated non-operatively with controlled early motion. The intervention group was allowed full WB from day 1. The control group was non-WB for 6 weeks. Primary outcome was the Achilles tendon Total Rupture Score (ATRS) after one year. Secondary outcomes were the Heel-rise-work-test, health related quality of life and the re-rupture rate (RR). Outcome-assessors were blinded to the intervention.

Results: 30 patients were randomized to each group; 29 and 27, respectively, were analyzed. There were no statistically significant differences between the WB and the non-WB groups at 12 months, except from a better health-related quality of life in the WB group (p=0.009). Mean ATRS at 12 months was 73 WB and 74 non-WB (p=0.81). The Heel-rise-work-test showed a total work performed of the injured limb compared to

the uninjured limb of 53% WB and 58% non-WB (p=0.37) at 12 months. There were 3 re-ruptures in the WB group and 2 RR in the non-WB (p=1.0).

Conclusion: There were no statistically significant differences between the groups in ATRS or Heel-rise-work-test, but an improved quality of life in the weight-bearing group. Both groups had significant functional deficits in the injured limb compared with the uninjured limb. Immediate weight-bearing is a recommendable option in the non-operative treatment of ATR.

Trial registration at ClinicalTrials.gov: NCT01470833. Limited grant support was received from DJO Nordic.

Level of evidence: Level 1

INTRODUCTION

Non-operative treatment of acute Achilles tendon rupture (ATR) is a well-accepted treatment modality used as the standard of care by approximately half of hospitals in some regions [1]. Dynamic rehabilitation after non-operative treatment of ATR has been suggested to be an important part of treatment yielding functional outcome and re-rupture rates comparable to that of surgically treated ATR [2345678]. However, the optimal non-operative treatment protocol remains to be clarified, particularly the role of weight-bearing during early rehabilitation.

ATR is a frequent and potentially disabling injury that typically occurs among young active adults (11 to 37 per 100,000 per year) [91011]. Consequently, optimizing treatment and shortening recovery holds the potential of socioeconomic benefits and improved functional outcome after ATR.

The role of controlled early motion has been discussed since the early 1980ies [23121314]. In theory, controlled early motion of tendons leads to a better and faster healing due to, inter alia, the release of growth factors [15], and animal studies have shown a three times increased strength of dynamic rehabilitated Achilles tendons [16]. Nonetheless, randomized Controlled trials comparing dynamic and immobilized rehabilitation protocols have found no important significant differences between groups. [1213141718].

The role of weight-bearing has been sparsely investigated in a clinical setup. In experimental models it is well documented that mechanical load improves tendon healing [15]. Thus, it is reasonable to believe that early loading of the tendon under controlled conditions will affect tendon healing beneficially. Immediate weight-bearing in a non-operative treatment protocol has been investigated in one randomized, controlled trial [14]. The trial provided no evidence of a functional benefit from immediate weight-bearing, but did not find any detrimental effect on outcome either. The trial suffered from methodological problems, as the

inclusion procedure led to selection bias with a skewed age distribution and further, the basic construct of the weight-bearing and non-weight-bearing regimes differed substantially. Early weight-bearing after surgery has been investigated in two randomized, controlled trials [1419]. The studies showed the weight-bearing groups to have an improved health related quality of life, a faster return to normal walking and no detrimental effect on other outcome parameters. The study by Costa et al. suffered from the methodological problems just mentioned.

The objective of this blinded, randomized, controlled trial was to compare immediate weight-bearing with non-weight-bearing in a non-operative treatment protocol for ATR using controlled early motion. We hypothesized that immediate weight-bearing would affect tendon healing positively and thus lead to a better patient reported and functional outcome. The primary endpoint was the Achilles tendon Total Rupture Score (ATRS) after one year.

MATERIAL AND PATIENTS

This was a blinded, randomized, controlled, superiority trial with participants individually randomized to one of two parallel groups. The trial was designed in accordance with the Consort requirements; no changes were made to the trial design after commencement of the trial. The full trial protocol can be acquired from the first author. The trial is registered at ClinicalTrials.gov, number NCT01470833. Limited grant support was received for the research from DJO Nordic. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Patients

Patients with ATR referred to the orthopedic department of Copenhagen University Hospital Hvidovre from April 2011 to March 2012 were assessed for eligibility. Diagnosis was based on a medical history with a clear snap of the Achilles tendon and a clinical examination with a palpable gap and positive Thompsons test [20]. Sixty patients were included in the trial and were randomly assigned to one of two parallel groups following a randomization procedure using opaque, sealed envelopes. The envelopes were prepared and shuffled by an experienced researcher with no other connection to the trial.

All patients aged 18 to 60 years who were expected to be able to follow the treatment protocol and give written consent in Danish were eligible for inclusion if randomization could be done within 4 days of the rupture. Exclusion criteria were previous Achilles tendon injury, corticosteroid injections within the last 6 months, ASA-score of three or more, medical history of arterial insufficiency in the legs and rupture within 1 cm of calcaneus. The rupture side was determined by palpation; in case of doubt ultrasound was used.

The study was approved by the Regional Ethical Review Board. All participants received oral and written information concerning the trial before written consent was obtained.

Treatment

Both groups received the following treatment: In the emergency department an ankle orthosis (DJO Nextep Contour2 Walker) with three wedges of 1.5cm was applied, fixating the ankle in equinus position (20-30 degrees of plantar flexion). The orthosis was worn for 8 weeks gradually bringing the ankle to neutral position by removing a wedge every second week (table 1). Patients were seen in the outpatient clinic after two and eight weeks. The patients were instructed not to remove the orthosis at any time during the first two weeks. After two weeks the first wedge was removed and controlled early motion begun: Patients were instructed to remove the orthosis at least 5 times a day sitting on the edge of a table with both legs hanging (figure 1). Gravity plantar flexed the foot and the patient actively dorsi flexed the foot to a horizontal position. Patients were instructed to do this in series of 25 repetitions. The orthosis was not to be removed except during exercises from week three to six. The last two weeks of treatment the orthosis could be removed at night.

Intervention

The treatment protocol for the intervention group was similar to that of the control group except for the permission to bear weight. The intervention group was allowed full weight-bearing from day one. Crutches were recommended but not obligatory the first two weeks of treatment. The control group was instructed not to bear weight for the first six weeks of treatment. The last two weeks full weight bearing was allowed. Compliance of the allocated regimen was controlled; as a pressure sensor was integrated in the orthosis and number of steps throughout the 8 week period was detected in both groups.

Rehabilitation

A standardized rehabilitation protocol was followed from week 9 to 16 where patients were trained three times a week by a team of specialized physiotherapists. Recommendations were individualized but in general cycling was allowed from week 10 and jogging from week 14. Racquet and contact sports could be resumed after one year other types of sports after six months.

Endpoints

Our primary endpoint was the Achilles tendon Total Rupture Score (ATRS) after one year. The ATRS is the only patient reported outcome measure validated for use after ATR [212223]. Secondary endpoints were the Heel-rise work test [24], re-rupture, length of sick leave and quality of life during treatment. The Heel-rise-work test was performed according to the instructions of Silbernagel et al. and Nilsson-Helander et al. [244]. The MuscleLab (Ergotest Technology, Oslo, Norway) was used and the patients were given standardized instructions: They warmed up for 5 minutes on a stationary bicycle with low load and did 3 sets of 10 two-legged toe raises. The uninjured side was tested first. Health related quality of life during the initial 8 weeks of treatment was measured using a purpose made 5 item Likert scale (range 0-10; 10 being the best possible score). The items reflected: 1) limitations in daily living, 2) limitations in work situations, 3) limitations in social life, 4) affection of the patient mood, and 5) level of pain.

Assessors and follow-up

Enrollment and allocation of treatment was done in the out-patient clinic, Copenhagen University Hospital Hvidovre, by the principal investigator or one of five orthopedic surgeons in close contact with the trial. Follow up at six and twelve months was done from October 2011 to March 2013 by two dedicated full time researchers at the Gait Analysis Lab, dep. of Orthopedic surgery, Copenhagen University Hospital Hvidovre. They were blinded to the intervention as they were not involved in the treatment and patients were instructed not to tell which group they had been allocated to. Follow up was organized in the following order: First the ATRS and other papers were filled out by the patient, then Heel-rise-work test was performed.

Statistical methods

Sample size calculation was done a priori: The clinical relevant difference in our primary endpoint (ATRS) was set to 10 points and the power to 0.90 (two sided). The standard deviation was estimated to 10 points from the material of Nilsson-Helander et al. [4]. Following these assumptions 22 patients were needed in each group. We included 30 patients in each group to account for patients lost to follow up.
Statistical analysis was performed following the intention to treat principles. The ATRS at one year was the primary end point of the study. Comparison between groups of continuous variables was done using the Mann-Withney U test, as our data did not follow the normal distribution. Comparison within groups was done using the Wilcoxon signed rank test. Comparison of groups by categorical data was performed using

the Fishers exact test. The level of significance was set at $p < 0.05$. The limb symmetry index (LSI) was calculated to compare the 2 treatment groups in the Heel-rise-work and Heel-rise-height. The LSI was defined as the ratio between the involved limb score and the uninvolved limb score, expressed as a percentage (involved/uninvolved x 100 = LSI) [4].

RESULTS

Thirty patients were randomly assigned to each group (figure 2). In the intervention group one patient discontinued the treatment and was lost to follow up as he decided for operative treatment in another hospital. In the control group two patients discontinued the treatment and were lost to follow up as they could not comply with the non-weight-bearing protocol and did not want to participate in the follow up. At half-year follow up one patient from each group did not show, as they were temporarily working out of the state. 28 patients from the intervention group and 27 from the control group were included in the half-year analysis, all belonging to their original assigned groups. At one year follow up a patient from the control group did not show as he was unsatisfied with the given treatment. 29 patients from the intervention group and 27 from the control group were included in the one-year analysis, all belonging to their original assigned groups.

Recruitment was done from April 2011 to March 2012. Recruitment was stopped when the planned number of patients had been enrolled. Follow up was done from October 2011 to March 2013.

Baseline demographic of the two groups is shown in table 2. Only minor differences were found between the two groups. The only statistically significant difference was the control group being on average 3 cm/ 1.2 inches taller.

Patient reported outcome

No statistically significant differences in ATRS were found between the weight-bearing and the non-weight-bearing group. The mean ATRS at 6 months follow up was 61.1 in the weight-bearing and 67.0 non-weight-bearing group, at 12 months it was 73.4 and 74.4, respectively (table 3). A statistically significant increase in ATRS was seen from 6 to 12 months in both groups ($p<0.001$ weight-bearing group, $p=0.009$ non-weight-bearing group).

Health related quality of life during the initial 8 weeks of treatment was significantly better in the group allowed immediate weight-bearing ($p=0.009$) (table 4).

Functional assessment

No statistically significant differences were found in heel-rise-work and heel-rise-height between the weight-bearing and the non-weight-bearing groups (table 3). The Heel-rise-work test showed a mean LSI at 6 months of 40% in the weight-bearing group and 36% in the non-weight-bearing group, after 12 months it was 53% and 58% respectively (table 3). A statistically significant increase in the Heel-rise-work test was seen from 6 to 12 months in both groups ($p<0.001$ for both groups).

Re-rupture

The overall rate of re-rupture was 5/57 (9%) at 12 month follow-up. Three re-ruptures were seen in the weight-bearing group and two in the non-weight-bearing (table 4). No statistically significant difference in re-rupture-rate was found between groups ($p=1.000$).

Work and sport

No statistically significant differences in length of sick leave and time to return to sports were found between groups (table 4). The mean length of sick leave was 52 days in the weight-bearing group and 58 in the non-weight-bearing ($p=0.580$). Sporting activities were resumed faster in the weight-bearing group (after mean 143 days) than in the non-weight-bearing (after mean 181 days), however it did not reach statistical significance ($p=0.358$) (table 4).

Complications

One patient in the non-weight-bearing group sustained a severe tendon elongation without a re-rupture. He had an operative tendon shortening but continued to have problems at one year follow up. No infections or nerve damages were seen in patients undergoing surgery due to re-rupture or elongation. No cases of deep venous thrombosis were found.

DISCUSSION

Dynamic rehabilitation has been advocated in a number of trend setting studies [2345]. However, the optimal non-operative treatment protocol for ATR remains to be clarified, particularly the role of early weight-bearing during dynamic rehabilitation. We hypothesized that immediate weight-bearing would affect tendon healing positively and thus lead to a better patient reported and functional outcome. This is the first RCT using validated outcome measures to investigate the role of immediate weight-bearing in a non-operative, dynamic rehabilitation protocol.

Non-operative treatment has gained increasing popularity during the past decade. A number of meta-analyses comparing operative and non-operative treatment have shown a significant lower rate of re-rupture and a significant higher rate of other complications among operatively treated patients [25768]. When looking only at studies using dynamic rehabilitation Soroceanu et al. found no significant difference in the rate of re-rupture between operatively and non-operatively treated patients; leaving the increased risk of other complications in the operative group to be the only statistically significant difference [6]. This correlates well with the postulate by Twaddle and Poon, that 'it is possible that controlled early motion is the important factor in optimizing outcomes in patients with Achilles tendon rupture and that surgery makes no difference to the outcome apart from increasing the risk of local infection' [3].
It should be noted, though, that the trials included in the meta-analysis by Soroceanu et al. differs from those included in the other meta-analyses. Also, it should be noted that no high quality trials have investigated the effect of controlled early motion compared to immobilization in a randomized controlled setup were the parallel groups differ only in the mobilization regime. And finally there is no broadly accepted definition of dynamic rehabilitation: In some studies it meant controlled early mobilization, in others controlled early weight-bearing and in others again a combination of the two. Also the mobilization regime differ, some used a hinged orthosis allowing continues movement where others used a fixed removable orthosis, like it was the case in this trial.

The role of weight-bearing is of fundamental importance as it influences not only the quality of treatment but also the patient ability to take care of oneself. Two previous RCT's have investigated the effect of weight-bearing in the treatment of ATR [1419]. Costa et al. considered return to normal activities as the most important outcome parameter. They found that immediate weight-bearing led to quicker return to normal walking and stair climbing in operatively but not in non-operatively treated patients [14]. Suchak et al. considered quality of life to be the most important outcome parameter. They found that early weight-bearing led to a better health-related quality of life during treatment. None of the studies found detrimental effects of early weight-bearing; they were, however, not designed as non-inferiority studies.

Our results show no statistically significant differences in ATRS or heel-rise-work test between groups. The study was powered to 0.90 based on the ATRS. The ATRS and Heel-rise-work test are measurements that have been specifically developed and validated for evaluation of ATR [212423]. The ATRS includes walking, stair climbing and questions related to quality of life. The combination of a patient reported outcome measure

and a functional endurance test has shown good validity and ability to detect changes to the condition [21,24] and includes the consideration of both Costa et al. and Suchak et al[14,19].

Health related quality of life during the initial eight weeks of treatment showed to be statistically significant better in the group allowed immediate weight-bearing. The improved health related quality of life in the immediate weight-bearing group might be explained by the practical advantages in daily living. Many of our patients in the intervention group expressed relief to be allowed weight-bearing as it left them less dependent on others. Our study brings further evidence to the conclusion of Suchak et al. that 'early weight-bearing provides enhanced quality of life'.

Re-rupture rate, time to return to work and time to return to sport showed differences that were, however, not statistically significant. The weight-bearing group experienced one extra re-rupture, returned to work averagely six days earlier and resumed sport 38 days earlier compared to the non-weight-bearing group. The idea of quicker return to work and sport after early weight-bearing due to less muscle atrophy is intriguing, but not answered in this trial, as the trial was not powered to show differences in those secondary outcomes.

Limitations

This study was designed as a superiority study intending to show that immediate weight-bearing was superior to non-weight bearing. As such the study cannot claim immediate- and non-weight-bearing to be equally effective in the treatment of ATR.

Compliance of the allocated regimen was controlled using a pressure sensor integrated in the orthoses. Unfortunately the pressure sensors broke during the treatment period. Patients, clinicians and assessors were not informed of this fact and the pressure sensors were used as sham devices. We did, however, not succeed to monitor compliance.

The power calculation in this study was based on a standard deviation of 10 points in ATRS, as was found in a the material of Nilsson-Helander et al. [4]. Our results showed a standard deviation of 16, which should be taken into consideration when designing future studies using the ATRS as primary outcome.

The generalizability of the study is good: we aimed to control for all other factors than weight-bearing and there was no recognized selection bias in the inclusion procedure. The results can be generalized to a population of healthy people between 18 and 60 years of age with no use of corticosteroids the past half year and no medical history of arterial insufficiency in the legs.

In future studies it would be interesting to investigate the role of controlled early motion in the rehabilitation after non-operative treatment of ATR. Controlled early motion has been strongly advocated as an important part of non-operative, dynamic rehabilitation [2345], but no high quality randomized, controlled trials has been forthcoming. It would also be interesting to look further into the influence of tendon length on return to normal gait-pattern using gait analysis. It has been shown in a case report using gait analysis, that the injured side displayed differences in strength, ankle range of motion, heel rise, and tendon length when compared to the uninvolved side 1 year after injury [26]. Finally it would be interesting to test the influence of immediate weight-bearing on a larger population to see if the found difference in time to return to work and sport as well as re-rupture rate is random or actual.

Conclusion

In conclusion it seems reasonable to recommend immediate weight bearing in a non-operative, dynamic treatment protocol as a safe treatment modality for ATR. Our results are consistent with previous findings. Immediate weight-bearing improves health related quality of life during treatment and does not seem to have detrimental effect on outcome.

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TABLES

Table 1 **Treatment protocol**
Week 1 and 2
Orthosis with three wedges.
The orthosis could not be removed at any time.
Intervention group: Weight-bearing allowed, crutches were recommended.
Control group: No weight-bearing.
Week 3 and 4
Orthosis with two wedges.
Controlled early motion in both groups.
Intervention group: Full weight-bearing.
Control group: No weight-bearing.
Week 5 and 6
Orthosis with one wedge.
Controlled early motion in both groups.
Intervention group: Full weight-bearing.
Control group: No weight-bearing.
Week 7 and 8
Orthosis without wedges.
Controlled early motion in both groups.
The orthosis could be removed at night.
Intervention group: Full weight-bearing.
Control group: Full weight-bearing.
Week 9 to 16
Visit to physiotherapist three times a week. Standardized rehabilitation protocol with room for individualization.

Table 2: Baseline demographic characteristics of the sample population

Variable	Weight-bearing	Non-weight-bearing	p-value
Age (years)	41.2 (6.4), 41.4 (26.6;51.8), n=29	39.1 (7.5), 39.2 (26.7;56.4), n=28	0.520
Gender (male/female)	24/5 (83%/17%)	24/4 (86%/14%)	1.000
Height (cm)	177.1 (7.0), 176.7 (163.5;196.7), n=27	180.0 (9.6), 178.1 (161.1;198.7), n=27	**0.041**
Weight	86.3 (13.7), 84.3 (63.2;116.2), n=27	86.1 (13.2), 86.4 (63.7;117.3), n=27	0.667
Injured side (right/left)	12/17 (41%/59%)	16/12 (57%/43%)	0.294
Dominant side (right/left)	21/3 (87%/13%)	18/3 (86%/14%)	1.000
Smoker (yes/no)	5/24 (17%/83%)	9/19 (25%/75%)	0.230
Work Heavy Light but mobile Sedentary	 8 (28%) 10 (34%) 11 (38%)	 5 (18%) 5 (18%) 18 (64%)	0.150
Sport (hours)	4.6 (2.4), 4.0 (1.0;10.0), n=22	5.5 (4.1), 5.0 (1.0;18.0), n=23	0.191
ATRS pre-injury	98.6 (4.0), 100 (79;100), n=29	98.7 (3.4), 100 (84;100), n=27	0.771

For categorical variables, data are reported as: n and (%). For continuous variables, data are reported as: mean (standard deviation), median (min; max), and n. The Fisher exact test was used for comparisons between groups of dichotomous variables. For continues, normally distributed variables the unpaired t-test was used. The Mann-Whitney U test was used for ATRS.

Table 3: Results

	6-month evaluation			12-month evaluation		
Test	Weight-bearing	Non-weight-bearing	p-value	Weight-bearing	Non-weight-bearing	p-value
ATRS	61.1 (18.0), 61 (34;95), n=28	67.0 (21.0), 67 (27;99), n=27	0.274	73.4 (16.2), 75 (39;94), n=29	74.4 (17.7), 75 (34;100), n=27	0.812
Heel-rise-work	40% (15), 42 (1;73), n=24	36% (21), 36 (1;72), n=24	0.464	53% (20), 53 (10;94), n=29	58% (25), 56 (9;99), n=25	0.372
Heel-rise height	66% (21), 67 (1;97), n=24	58% (23), 65 (0;96), n=24	0.240	69% (17), 70 (26;96), n=29	72 (14), 73 (42;95), n=25	0.440

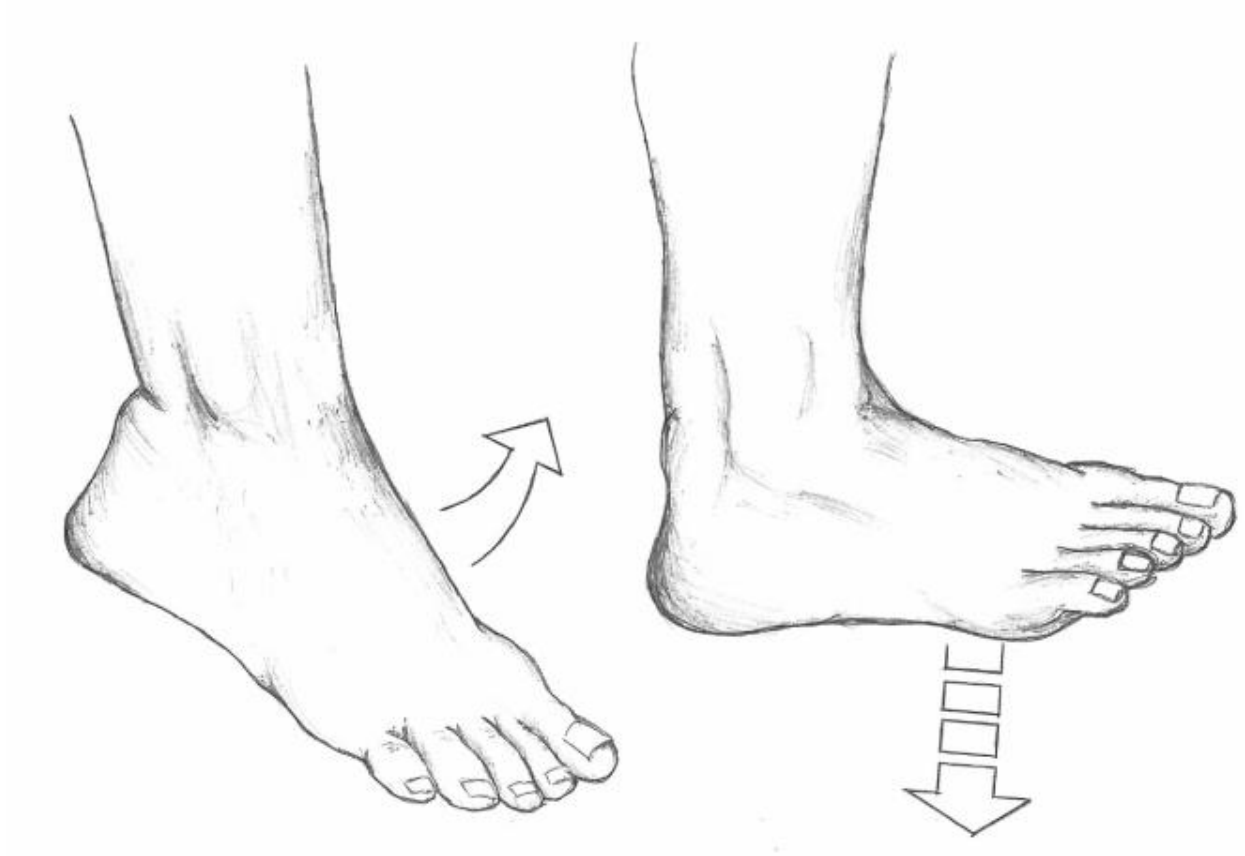
Data are reported as: mean (standard deviation), median (min; max), and n. The limb symmetry index (LSI) was calculated to compare the 2 treatment groups in the functional tests. The LSI was defined as the ratio between the involved limb score and the uninvolved limb score, expressed as a percentage (involved/uninvolved x 100 = LSI). The Mann-Whitney U test was used to evaluate differences between groups.

Table 4: Results

Test	Weight-bearing	Non-weight-bearing	p-value
Quality of life during treatment	6.3 (1.8), 6.6 (3;9), n=29	5.0 (5.0), 1.8 (1;8), n=27	**0.009**
Re-rupture (yes/no)	3/29 (10%/90%)	2/27 (7%/93%)	1.000
Sick leave (days)	52 (67), 9 (1;221), n=25	58 (48), 48 (0;144), n=25	0.580
Resumption of sports (days)	143 (44), 145 (81;226), n=24	181 (98), 151 (62;415), n=20	0.358

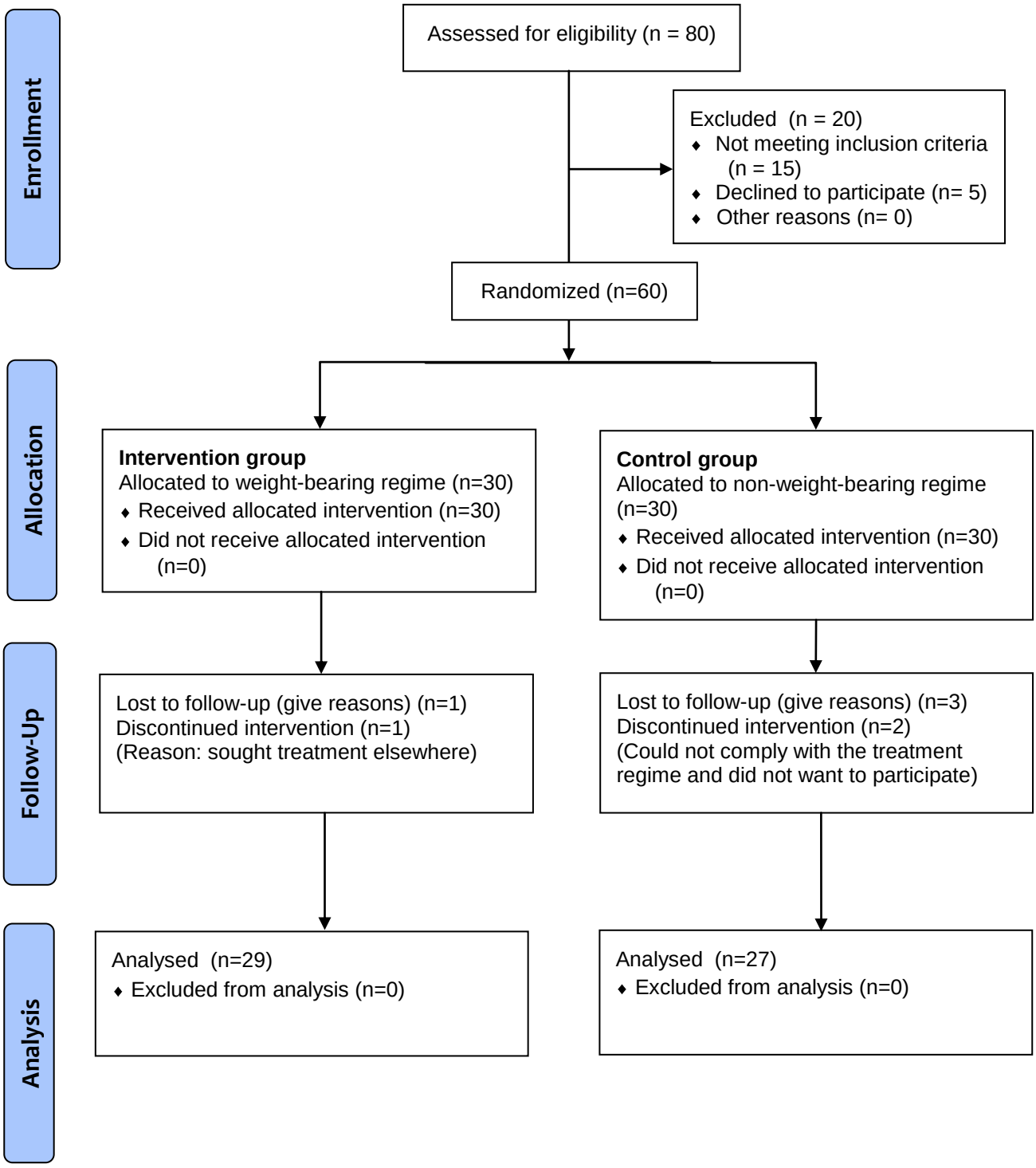
For categorical variables, data are reported as: n and (%). For continuous variables, data are reported as: mean (standard deviation), median (min; max), and n. The Fisher exact test was used for comparisons between groups of dichotomous variables. For continues variables the Mann-Whitney U test was used.

Figure 1



Controlled early motion: The patients in both groups did controlled early motion of the ankle joint from week 3 to 8. Patients were instructed to remove the orthosis at least 5 times a day sitting on the edge of a table with both legs hanging. Gravity plantar flexed the foot where upon the patient actively dorsi flexed the foot to a horizontal position. Patients were instructed to do this in series of 25 repetitions

FIGURE 2: Consort Flow Diagram



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Non-operative, dynamic treatment of acute Achilles tendon rupture: The influence of early weight-bearing on biomechanical properties of the plantar-flexor muscle-tendon complex. A blinded, randomized, controlled trial.

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Non-operative, dynamic treatment of acute Achilles tendon rupture: The influence of early weight-bearing on biomechanical properties of the plantar-flexor muscle-tendon complex. A blinded, randomized, controlled trial.

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ABSTRACT

Background: Acute Achilles tendon rupture (ATR) causes damage to the fibrous structure of the tendon. The altered biomechanical properties of the plantarflexor muscle-tendon complex (PMTC) may have consequences for functional performance and risk of re-injury.

Purpose: To compare the biomechanical properties of the PMTC of both limbs in patients randomized to early weight-bearing (WB) or non-WB in non-operative treatment of ATR.

Study Design: Randomized Controlled Clinical Trial.

Methods: Sixty patients were randomized into two groups. In both groups, patients were treated non-operatively with dynamic rehabilitation. The intervention group was allowed full WB from day 1 of treatment. The control group was non-WB for 6 weeks. After 6 and 12 months the peak passive torque at 20 degrees dorsiflexion and stiffness during slow stretching in early, medium and late dorsiflexion were measured in both the affected and unaffected limb. Likewise, the maximal strength (plantarflexor torque at 20 degrees dorsiflexion) was investigated in both limbs. Data was evaluated using T-tests.

Results: There were no significant differences between the WB and the non-WB groups. Compared to the unaffected limb, peak passive torque was significantly lower for the affected limb at 6 months (91%, p=0.01), not at 12 months (98%, p=0.51). Stiffness was significantly lower for the affected limb during the

early part of dorsiflexion at 6 months (67%, p<0.001), and remained inferior at 12 months (77%, p<0.001). Irrespectively of group, the strength was significantly lower in the affected compared to the unaffected limb at both 6 (82%, p<0.001) and 12 months (93%, p=0.009).

Conclusion: There were no significant effects of treatment regimens on the biomechanical properties of PMTC. The reduced stiffness and strength in the affected limb in the early part of dorsiflexion may have substantial implications for coordination of i.e. gait and running, and the fact that the stiffness is not normalized after 12 months may indicate a need for better treatment and rehabilitation.

INTRODUCTION

Achilles tendon rupture is a frequent and potentially disabling injury that typically occurs among young active adults (11 to 37 per 100,000 per year).[10,12,17] Achilles tendon rupture causes damage to the fibrous structure of the tendon. The organized architecture of the collagen fibers is lost, and an increased content of type III collagen is seen at the rupture site.[9,11,20,27] An average elongation of the tendon of 2.5-3.5cm has been described after Achilles tendon rupture in humans, and a linear relationship between tendon elongation and functional deficits has been proposed. [22,25] The remodeling of the plantar flexor muscle-tendon complex during healing leads to changes in biomechanical properties that likely affect functional performance and risk of re-injury.[13,26,15] An uninjured Achilles tendon works as a shock absorber storing and releasing energy during gait and running. The ability to do so depends on its elastic properties: stiffness, energy stored and torque relaxation.[4,18] Also the risk of re-injury depends on the tendons elastic properties as the load to failure is determined by the tendons stiffness and maximal energy stored.[18]

Non-operative treatment using early weight-bearing is a well-accepted treatment modality for acute Achilles tendon rupture used as the standard of care by approximately half of hospitals in some regions.[2,14] It is likely that weight-bearing during early rehabilitation of acute Achilles tendon rupture affects tendon healing and thus its biomechanical properties. In experimental models mechanical loading of healing tendons has shown beneficial in terms of an increased load to failure and an increased stiffness.[1,20] In a randomized controlled trial McNair et al. allocated 38 non-operatively treated Achilles tendon ruptures to a non-weight bearing protocol and a weight bearing protocol.[15] At 6 months follow up they found weight-bearing to be beneficial, as the group allowed early weight-bearing showed higher stiffness and energy stored than the non-weight-bearing group.

Looking at functional outcomes, early weight-bearing has been investigated in three randomized, controlled trials: One testing a non-operative treatment protocol[7], and two testing surgical treatment

protocols.[7,24] The trials showed a faster return to normal walking and an improved quality of life in the groups allowed weight-bearing. This is the first randomized controlled trial to investigate how the biomechanical properties of the plantar flexor muscle-tendon complex are influenced by early weight-bearing at one year follow up.

The objective of this blinded, randomized, controlled trial was to compare the biomechanical properties of the plantar flexor muscle-tendon complex of both limbs in patients randomized to early weight-bearing or non-weight-bearing. Both groups were treated non-operatively using controlled early mobilization. Peak passive torque, stiffness, energy stored and strength one year after rupture were the endpoints of interest in this study.

MATERIAL AND PATIENTS

This study is based on data from a blinded, randomized, controlled trial with participants individually randomized to one of two parallel groups. Both functional and biomechanical data were collected. Only biomechanical data are presented in this paper. The trial was designed in accordance with the Consort requirements; no changes were made to the trial design after commencement of the trial. The full trial protocol can be acquired from the first author. The trial is registered at ClinicalTrials.gov, number NCT01470833. Limited grant support was received for the research from DJO Nordic. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Patients

Enrollment and allocation of treatment was done in the out-patient clinic, Copenhagen University Hospital Hvidovre, by the principal investigator or one of five orthopedic surgeons in close contact with the trial. Patients referred to the department with acute Achilles tendon rupture in the period from April 2011 to March 2012 were assessed for eligibility. Diagnosis was based on a medical history with a clear snap of the Achilles tendon, a clinical examination with a palpable gap and positive Thompsons test.[28] Sixty patients were included in the trial. They were randomized using opaque, sealed envelopes to one of two parallel groups. An experienced researcher with no other connection to the trial prepared and shuffled the envelopes.

Patients aged 18 to 60 years who were expected to be able to follow the treatment protocol and give written consent in Danish were eligible for inclusion if randomization could be done within 4 days of the rupture. Exclusion criteria were previous Achilles tendon injury, corticosteroid injections within the last 6 months, American Society of Anesthesiologists (ASA)-score[6] of three or more, medical history of arterial

insufficiency in the limbs and rupture within 1 cm of calcaneus. The location of rupture was determined by palpation; in case of doubt ultrasound was used. The study was approved by the Regional Ethical Review Board. Oral and written consent was obtained from all participants.

Treatment and intervention

In the emergency department an ankle orthosis (DJO Nextep Contour2 Walker) with three wedges of 1.5cm was applied, fixating the ankle in 20-30 degrees of plantar flexion. The ankle was gradually brought to neutral position over the following 8 weeks by removing a wedge every second week. Controlled early motion was begun after 2 weeks. The control group was instructed not to bear weight for the first six weeks of treatment. The last two weeks, full weight bearing was allowed.

The intervention group differed from the standard treatment protocol as full weight-bearing was allowed from day one. Crutches were recommended but not obligatory the first two weeks of treatment. Compliance of the allocated regimen was controlled; as a pressure sensor was integrated in the orthosis and number of steps throughout the 8 week period was detected in both groups.

A standardized rehabilitation protocol was followed from week 9 to 16 where patients were trained three times a week by a team of specialized physiotherapists. In general cycling was allowed from week 10 and jogging from week 14, but recommendations were individualized. Sports could be resumed after six months, but patients were advised not to resume racquet and contact sports before 12 months.

Assessors and follow-up

Follow up was done from October 2011 to March 2013 by two dedicated full time researchers at the Gait Analysis Lab, dep. of Orthopedic surgery, Copenhagen University Hospital Hvidovre. They were blinded to the intervention as they were not involved in the treatment and patients were instructed not to tell which group they had been allocated to.

Procedures

Follow up was done at six and twelve months; the primary endpoint being at twelve months. A clinical and a biomechanical assessment were performed. Measurements of passive tension in the plantar flexor muscle-tendon complex were performed using an isokinetic dynamometer. A motor (Caldercraft Electric Motors, model 26) was driven by a DC power amplifier (model 2708; Brüel & Kjær, Naerum, Denmark) and

could deliver maintained torques up to 80Nm and peak torques up to 120Nm. An electro-goniometer, connected to the footplate, measured the angle of the ankle joint and a torque meter measured the torque exerted on the footplate. This apparatus was developed and shown to produce highly reproducible measurements of passive and reflex-mediated torque around the ankle joint by Toft et al. and Sinkjær et al.[29,31] Before testing in the isokinetic dynamometer the patient warmed up on a stationary bicycle for 5 minutes. For the measurements the patient was positioned with the foot strapped to a pedal in 10 degrees of plantar flexion and the knee and hip fixed in 90 degrees flexion. Patients were asked to relax and not activate their calf muscles as the ankle was passively moved into dorsiflexion by the pedal at an angular velocity of 5 degrees/sec. The isokinetic dynamometer rested for 2 seconds at maximal dorsiflexion before the pedal was returned to the starting position at the same velocity. The resistant torque was sampled at a frequency of 1000Hz. Patients who had a ROM exciding 20 degrees of dorsiflexion were tested in the range from 10 degrees plantar-flexion to 20 degrees dorsiflexion. Seven patients had a range of motion below 20 degrees of dorsiflexion, they were tested in the range from 20 degrees plantar-flexion to 10 degrees dorsiflexion. Ten repetitions were performed on each limb. The unaffected limb was tested before the affected.

Strength was measured using the same isokinetic dynamometer setting. The patient was asked to relax as the dynamometer dorsiflexed their ankle to 10 or 20 degrees of dorsiflexion, respectively. The dynamometer rested for 3 seconds and the patient was encouraged to deliver maximal plantar-flexion power without activating the thigh while the dynamometer plantar flexed the foot 40 degrees from the starting position with a speed of 6.7°/s. Five repetitions were performed on each limb. The unaffected limb was tested before the affected. Standardized verbal encouragement was provided to ensure maximal effort.[16]

Data analysis and processing

Data was processed using a Butterworth 4th order lowpass filter with a cutoff frequency at 2 Hz. Concerning the biomechanical data, the average of the median two repetitions was used for further analysis. The peak passive torque was measured at maximal dorsiflexion (10 or 20 degrees, respectively). Stiffness was determined as the increase in passive torque per degree of dorsiflexion (DF) by obtaining the maximal stiffness in the early (max-DF minus 22.5° to max-DF minus 14°), middle (max-DF minus 14° to max-DF minus 7.5°) and late (max-DF minus 7.5° to max-DF) part of the dorsiflexion. Energy stored during loading was calculated as the area under the loading curve as described by McNair et al.[15]. The torque relaxation of the tendon during the two second period of maximal tension was calculated as the absolute

relaxation divided by the peak passive torque as described by Bressel et al. [4]. Concerning the strength data, the first repetition was considered a trial attempt and excluded. The three repetitions with the highest strength measures were selected and the average values for the measuring angles were calculated for further analysis. Measuring angles were 20° of dorsiflexion, 10° of dorsiflexion, neutral, 10° of plantar flexion and 20° of plantar flexion.

Statistical analysis

Sample-size calculations were made on a primary endpoint not presented in this paper. If, however, one would make a post-hoc sample-size calculation on the biomechanical data, we suggest using peak passive torque as endpoint. Bressel et al. estimated the clinical relevant difference to 15% of the normal value, equaling 4.5Nm in their material[4]. Their data had a standard deviation of 6 Nm. Setting the power to 0.80 (two sided) 28 patients would be needed in each group.

Statistical analysis was performed following the intention to treat principles. Comparison between and within groups was done using unpaired and paired t-test, respectively. Repeated measurements were analyzed using repeated measurement analysis of variance. The limb symmetry index (LSI) was calculated to compare the two treatment groups. The LSI was defined as the ratio between the affected limb and the unaffected limb, expressed as a percentage (involved/uninvolved x 100 = LSI).[19]

RESULTS

Thirty patients were randomly assigned to each group (figure 1). In the intervention group one patient discontinued the treatment and was lost to follow up as he decided for operative treatment in another hospital. In the control group two patients discontinued the treatment and were lost to follow up as they could not comply with the non-weight-bearing protocol and did not want to participate in the follow up. At half-year follow up two patients from the intervention group and five patients from the control group were not tested due to technical problems with the isokinetic dynamometer. 27 patients from the intervention group and 23 from the control group were included in the half-year analysis, all belonging to their original assigned groups. At one year follow up two patients from the intervention group and seven patients from the control group were not tested due to technical problems with the isokinetic dynamometer. Furthermore one patient from the intervention group did not participate due to pain in the tendon and one patient from the control group did not show as he was unsatisfied with the given treatment. 26 patients from the intervention group and 20 from the control group were included in the one-year analysis, all belonging to their original assigned groups. Recruitment was done from April 2011 to March 2012. Follow

up was done from October 2011 to March 2013. Baseline demographic of the two groups is shown in table 1.

Stiffness

There were no significant differences in peak passive torque and stiffness between the weight-bearing and the non-weight-bearing groups (table 2). Comparing the affected and unaffected limb, peak passive torque was statistically significantly lower in the affected limb at 6 months follow up (87%, p=0.010) but not at 12 months follow up (97%, p=0.511) (table 3). A statistically significantly lower stiffness was found for the affected limb during the early part of dorsiflexion at 6 months (67%, p<0.001), and remained inferior at 12 months (77%, p<0.001) despite statistically significant improvement over time (p=0.019) (table 3). Comparing the three consecutive stiffness measurements using repeated measurement analysis of variance, no difference was found between the affected and unaffected limb at 6 (p=0.628) or 12 months (p=0.663).Increasing stiffness was observed with increasing dorsiflexion (table 3).

Energy stored and torque relaxation

There were no statistically significant differences in energy stored during loading or torque relaxation of the muscle-tendon complex between the weight-bearing and the non-weight-bearing groups (table 2). Comparing the affected and unaffected limb, a statistically significant decrease in the ability to store energy was seen in the affected limbs at both 6 (74%, p<0.001) and 12 months (82% p<0.001) follow up (table 3). Likewise, a statistically significant increase in torque relaxation was found in the affected limbs at both 6 (114%, p<0.001) and 12 months (111% p<0.001) follow up (table 3).

Strength

The limb symmetry index (LSI) showed a statistically significantly lower maximal strength in the weight-bearing group compared to the non-weight-bearing group at 6 months (87%, p=0.027) but not at 12 months (96%, p=0.534) (table 2). However, when looking at the absolute strength values, the unaffected limb was significantly stronger in the weight-bearing group at 6 months (117%, p=0.035), but not at 12 months (114%, p=0.11), whereas no difference was found between groups in the affected limb (table 2). Irrespectively of group, the maximum strength was significantly lower in the affected compared to the unaffected limb throughout range of motion at both 6 (82%, p<0.001) and 12 months (93%, p=0.009) (table 3), and the same trend was seen throughout range of motion (6 months p<0.001; 12 months p=0.002) (figure 2).

DISCUSSION

Achilles tendon rupture causes damage to the fibrous structure of the tendon leaving the healed tendon with altered architecture. The remodeling of the tendon leads to changes in biomechanical properties that likely affect functional performance and risk of re-injury. We hypothesized, that weight-bearing during early rehabilitation of acute Achilles tendon rupture would affect tendon healing and thus its biomechanical properties.

Our results show no statistically significant differences in biomechanical properties of the muscle-tendon complex between the weight-bearing and non-weight-bearing groups at 6 or 12 months follow up (table 2). These findings are contrary to the findings of McNair et al.[15] who found a significantly higher peak passive torque and energy stored in the weight-bearing group at 6 months follow up. Irrespectively of group allocation, significant deficits were seen in the affected limb at both 6 and 12 months follow up (table 3); indicating reduced function of the Achilles tendon one year after injury. When interpreting the deficits, the assumption by Bressel et al., that only differences above 15% are clinical relevant, must be kept in mind.[4] The affected limb had statistically significantly lower, but not clinically relevant, peak passive torque at 6 months (87%, p=0.010) that was normalized at 12 months (table 3). At both 6 (67%, p<0.001) and 12 months (77%, p=0.001) a statistically significant and clinically relevant reduced stiffness was found in early part of dorsiflexion in the affected limb. Likewise, a statistically significant and clinically relevant decrease in energy storage capacity of the plantar muscle-tendon complex was seen in the affected limbs at both 6 (74%, p<0.001) and 12 months (82% p<0.001) follow up (table 3). Torque relaxation was statistically significantly increased at both 6 (114%, p<001) and 12 months (111%, p<001), but the differences were not clinically relevant (table 3). McNair et al. have found similar differences between affected and unaffected limbs at 6 months follow up[15], and Don et al. found reduced stiffness at 3 and 6 months follow that was normalized at 12 months[8]. At long term follow up Bressel et al. did not find significant impairments in biomechanical properties 1-5 years after rupture.

Persisting deficits may affect performance in activities involving the stretch-shortening cycle[5], as it has been demonstrated, that up to 60% of work involved in repetitive jumping exercises is generated in the tendon.[30] Furthermore the reduced stiffness in the early part of dorsiflexion and the increased torque relaxation may have substantial implications for coordination of i.e. gait and running. Bressel et al. have shown unilateral changes in stiffness and torque relaxation after Achilles tendon rupture to be correlated with deficits in tendon proprioception in both limbs.[3] The fact that stiffness and energy storage capacity of the plantar

muscle-tendon complex is not normalized after 12 months may indicate a need for better treatment and rehabilitation.

Our strength data showed a significantly higher, but not clinically relevant, LSI for the non-weight-bearing group at 6 months (87%, p=0.027), not at 12 months (96%, p=0.534) (table 2). The relative difference at 6 months was, however, most likely due to decreased muscle atrophy in the unaffected limb in the group allowed immediate weight-bearing; as the unaffected limb was statistically significantly stronger in the weight-bearing compared to the non-weight-bearing group, whereas no difference was found in the affected limb (table 3). Irrespectively of group allocation, statistically significant strength deficits were seen in the affected limb at 6 (82%, p<0.001) and 12 months (93%, p=0.009) (figure 5). Our results are comparable to other biomechanical studies that have found strength deficits ranging between 10% and 20%.[4,15] In comparison to functional strength and endurance tests the deficits are markedly small. Evaluating patients using the heel-rise-work test, deficits between 25% and 40% are reported in the affected limb.[21]

Limitations

This study is based on data from a blinded, randomized, controlled trial powered to analyze a primary outcome not presented in this paper. A post-hoc sample-size calculation using peak passive torque as endpoint reveals the study to be adequately powered for our purpose. However, the large spread of data and the 23% (14/60) lost to follow up impairs our possibility to detect actual differences. The spread of data can be due to normal variation between patients, procedural imprecision in the biomechanical testing or malfunction of the isokinetic dynamometer. As malfunctioning of the isokinetic dynamometer is unlikely, the spread of data must be explained by to the first two factors.

It should also be noted that we did not succeed to monitor compliance of the allocated regimen as planned, as the pressure sensors broke during the treatment period. Patients, clinicians and assessors were not informed of this fact and the pressure sensors were used as sham devices.

The generalizability of the study is acceptable: we aimed to control for all other factors than weight-bearing and no selection bias were recognized in the inclusion procedure. However, due to technical problems 10 out of 30 included patients were lost to follow up in the control group.

In future studies it would be interesting to look further into the correlation between tendon length, biomechanical properties of the muscle-tendon complex and the return to normal gait-pattern using gait analysis. The combination of gait analysis and biomechanical testing would help us better define clinical

relevant values for the biomechanical endpoints. Gait analysis has shown that improvement of gait pattern is slower than recovery of plantar flexor mechanical properties[8], and that the injured side displayed differences in strength, ankle range of motion, heel rise, and tendon length when compared to the uninvolved side one year after injury.[23] Finally it would be interesting to test the influence of immediate weight-bearing on a larger population.

Conclusion

In conclusion it seems reasonable to recommend immediate weight bearing in a non-operative, dynamic treatment protocol as a safe treatment modality for acute Achilles tendon rupture, as no significant effects of weight-bearing on the biomechanical properties of the plantar muscle-tendon complex were found. The reduced stiffness and strength in the affected limb in the early part of dorsiflexion may have substantial implications for coordination of i.e. gait and running, and the fact that the stiffness is not normalized after 12 months might indicate a need for better treatment and rehabilitation.

Table 1: Baseline demographic characteristics of the sample population

Variable	Weight-bearing	Non-weight-bearing	p-value
Age (years)	41.2 (6.4), n=29	39.1 (7.5), n=28	0.520
Gender (male/female)	24/5 (83%/17%)	24/4 (86%/14%)	1.000
Height (cm)	177.1 (7.0), n=27	180.0 (9.6), n=27	**0.041**
Weight	86.3 (13.7), n=27	86.1 (13.2), n=27	0.667
Injured side (right/left)	12/17 (41%/59%)	16/12 (57%/43%)	0.294
Dominant side (right/left)	21/3 (87%/13%)	18/3 (86%/14%)	1.000
Smoker (yes/no)	5/24 (17%/83%)	9/19 (25%/75%)	0.230

For categorical variables, data are reported as: n and (%). For continuous variables, data are reported as: mean (standard deviation), and n. The Fisher exact test was used for comparisons between groups of dichotomous variables. For continues, normally distributed variables the unpaired t-test was used.

Table 2: Results comparing weight-bearing and non-weight-bearing groups

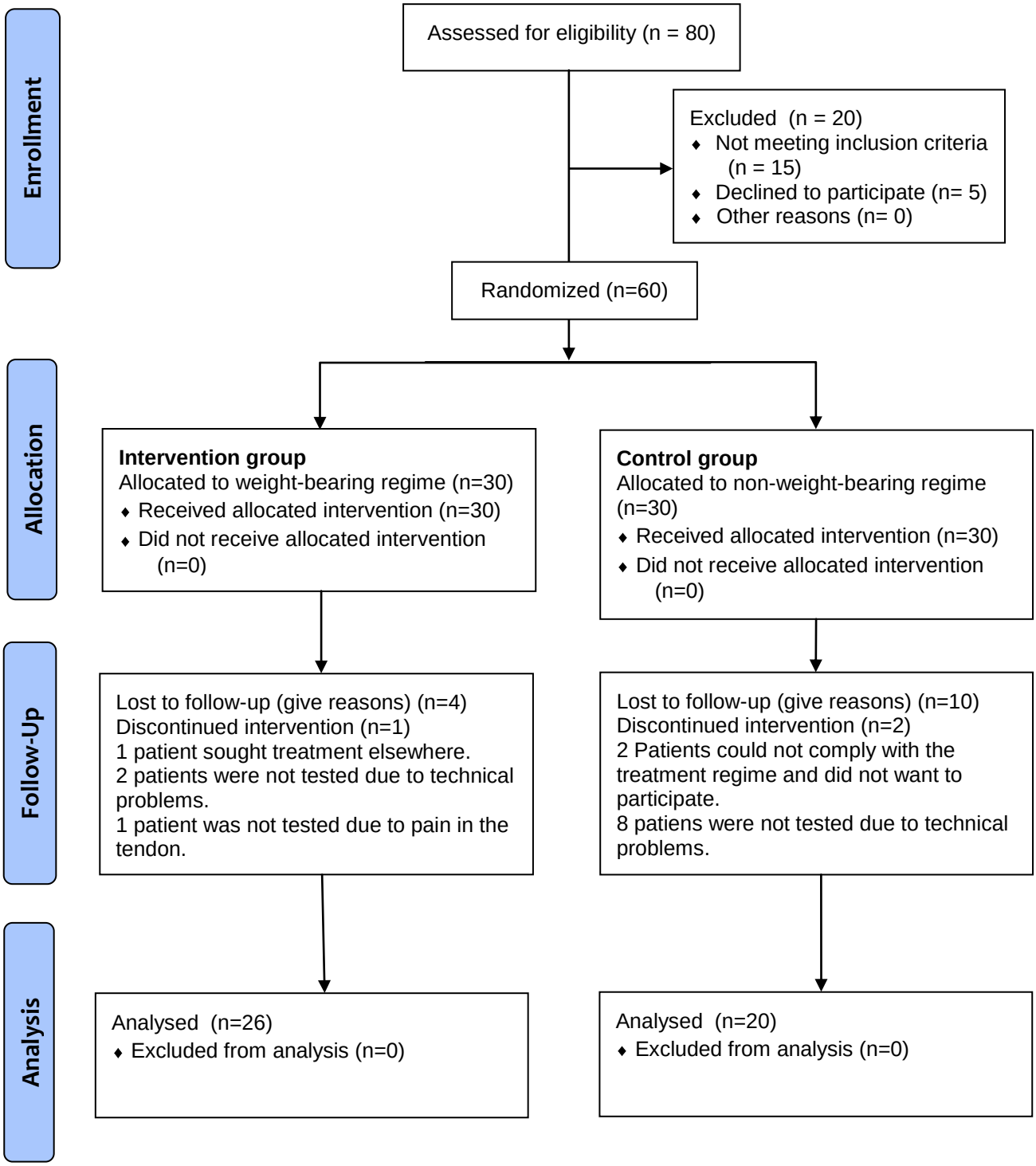
	6-months evaluation			12-months evaluation		
Test	Weight-bearing	Non-weight-bearing	Relative difference	Weight-bearing	Non-weight-bearing	Relative difference
Peak passive torque – (LSI)	89.8 (30.0), n = 27	91.2 (42.4), n=23	98% p=0.137	91.3 (28.1), n=26	108.1 (30.5), n=20	84% p=0.722
Stiffness in early ROM – (LSI)	69.2 (21.1), n = 27	70.2 (32.3), n=23	99% p=0.097	75.8 (24.7), n=26	86.4 (31.3), n=20	88% p=0.529
Stiffness in middle ROM – (LSI)	94.8 (35.9), n = 27	96.1 (47.0), n=23	99% p=0.258	97.9 (35.1), n=26	111.0 (35.5), n=20	88% p=0.830
Stiffness terminal ROM – (LSI)	99.1 (41.8), n = 27	107.4 (56.5), n=23	92% p=0.449	103.2 (35.0), n=26	82.7 (33.7), n=20	125% p=0.697
Torque relaxation (LSI)	115.1 (16.5), n = 27	114.0 (22.0), n=23	101% p=0.841	110.9 (16.2) , n=26	114.5 (24.3) , n=20	97% p=0.577
Energy stored (LSI)	72.8 (16.4), n=26)	69.5 (20.2), n=21	105% P=0.538	79.1 (20.2), n=26	90.0 (21.6), n=20	88% p=0.119
Max strength (LSI)	76.9 (16.8) , n=25	88.7 (17.9) , n=22	87% **p=0.027**	92.9 (21.6) , n=26	97.1 (22.6) , n=19	96% p=0.534
Max strength affected limb (Nm)	80.7 (28.7) , n=25	74.1 (25.1), n=22	109% p=0.414	95.7 (28.7), n=26	87.1 (27.7), n=19	110% p=0.315
Max strength unaffected limb (Nm)	101.6 (32.2), n=27	87.1 (25.5), n=22	117% **p=0.035**	104.6 (27.8) , n=26	91.4 (27.1) , n=20	114% p=0.113

Data are reported as: mean (standard deviation), number of patients. The limb symmetry index (LSI) was calculated to compare the 2 treatment groups. The LSI was defined as the ratio between the involved limb score and the uninvolved limb score, expressed as a percentage (involved/uninvolved x 100 = LSI). The unpaired t-test was used to evaluate differences between groups. Relative difference = affected/unaffected.

Table 3: Results comparing affected and un-affected limb

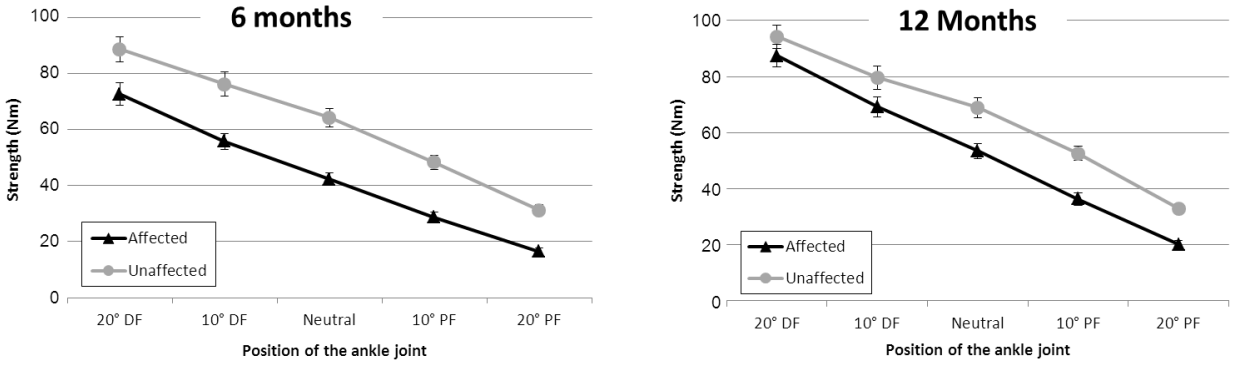
	6-months evaluation			12-months evaluation		
Test	Affected	Un-affected	Relative difference	Affected	Un-affected	Relative difference
Peak passive torque (Nm)	11.07 (5.3), n=50	12.78 (5.9), n=50	87% **p=0.010**	13.49 (6.2), n=46	13.96 (5.5), n=46	97% p=0.511
Stiffness in early ROM (Nm/°)	0.240 (0.11), n=50	0.358 (0.13), n=50	67% **p<0.001**	0.324 (0.14), n=46	0.422 (0.18), n=46	77% **p<0.001**
Stiffness in middle ROM (Nm/°)	0.520 (0.28), n=50	0.568 (0.28), n=50	92% p=0.144	0.651 (0.35), n=46	0.638 (0.28), n=46	102% p=0.740
Stiffness terminal ROM (Nm/°)	1.124 (0.59), n=42	1.038 (0.59) , n=42	108 p=0.236	1.330 (0.69), n=46	1.153 (0.57), n=46	115% **p=0.017**
Torque relaxation (%)	14.8 (2.1), n=42	13.0 (1.59), n=42	114% **p<0.001**	14.3 (1.7), n=46	12.9 (1.8), n=46	111% **p<0.001**
Energy stored (KJ)	21.49 (9.4), n=50	28.89 (11.4), n=50	74% p<0.001	26.09 (10.5), n=46	31.65 (10.9), n=46	82% p<0.001
Max strength (Nm)	77.6 (27.0), n=47	94.4 (31.2), n=47	82% **p<0.001**	92.1 (28.3), n=45	99.0 (28.3), n=45	93% **p=0.009**
Data are reported as: mean (standard deviation), number of patients. The paired t-test was used to evaluate differences between limbs. Relative difference = affected/unaffected.						

FIGURE 1: Consort Flow Diagram



Legend: **Consort flow diagram:** Showing the flow of patients from inclusion to final follow up.

FIGURE 2: Strength in the affected limb compared to the unaffected limb at 6 and 12 months.



Legend: Graphs showing strength throughout range of motion in the affected and unaffected limb at 6 and 12 months. P-values for the comparison of affected and unaffected limb using repeated measurement ANOVA: 6 months $p<0.001$; 12 months $p=0.002$. DF=dorsiflexion, PF=plantarflexion.

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IV

Validation of a Novel Ultrasound Measurement of Achilles tendon Length and Elongation.

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ABSTRACT

Purpose: Elongation of the Achilles tendon after acute rupture is associated with inferior functional outcome. A clinically applicable and accurate method for evaluating Achilles tendon elongation is needed. The purpose of this study was to develop and validate an ultrasonographic (US) method that accurately measures the length of the Achilles tendon-aponeurosis complex.

Material and methods: Both legs of 19 non-injured subjects were examined by MRI and US. The length of the Achilles tendon-aponeurosis complex (calcaneus to the medial head of m. gastrocnemius) was measured by three independent US examiners. Repeated US measurements were performed and compared to MRI measurements. Intra-rater and inter-rater reliability and the agreement between MRI and US was determined. Data were evaluated using the Intraclass Correlation Coefficient (ICC), the Standard Error of the Measurement SEM) and the Minimal Detectable Change (MDC).

Results: Intra-rater reliability of US assessment showed no significant differences between test days (p=0.45); ICC 0.96, SEM 3.7mm and MDC 10.3mm. Inter-rater reliability showed a systematic difference between US observers of 2.1mm – 4.5mm (p=0.001-0.036); ICC 0.97, SEM 3.3mm and MDC 9.3mm. MRI measurements were on average 3.8mm longer than US (p=0.001); ICC 0.98, SEM 2.7mm and MDC 7.6mm.

Conclusion: The novel ultrasound measurement showed excellent reliability. For comparison between groups of non-injured subjects differences of more than 4mm can be detected. For repeated assessment of individual subjects differences of more than 10mm can be detected. This new ultrasound measurement is a promising clinical tool to be further assessed in the setting of acute Achilles tendon rupture.

INTRODUCTION

Patients acquiring an acute Achilles tendon rupture (ATR) are affected for the rest of their life [6]. Most patients return to normal activities of daily living and 30% - 66% resume previous sporting activities, however, a considerable group of patients suffer from persistent unacceptably decreased functional outcome [16] [13]. Elongation of the Achilles tendon after acute rupture is well known and associated with inferior clinical outcome [9][24]. Therefore, it is desirable to identify the group of patients in high risk of elongation in the acute or early phase after ATR in order to individualize and thus optimize their treatment. A clinically applicable, accurate and easy to perform method for evaluating Achilles tendon length and elongation is needed.

Inferior results after ATR are correlated with complications like infection, surgical adhesion, nerve damage and tendon elongation [14][17][10][25][8][7]. Biomechanical studies have found loss of plantar flexion power after ATR [15] and clinical studies have found a decreased maximal heel-rise height after ATR to be correlated with Achilles tendon elongation and inferior clinical outcome [24].

Different methods to measure Achilles tendon elongation have been developed [1][4][9][11][18][19][21] [22][26][30]. The methods can be divided into four groups depending on modality: X-ray, ultrasonographic (US), Magnetic Resonance Imaging (MRI) and clinical. X-ray allows for measurement of displacement of the torn tendon ends by implantation of radiological markers [4][9]. The latest and best validated method is Roentgen Stereophotogrammetric Analysis (RSA) using tantalum beads as markers [22][11]. Because implantation of markers is invasive the technique has only been used to evaluate elongation after operative treatment.

US has been established as an important and cost-effective tool in the diagnosis of tendon problems. Rees et al. developed a method combining video-based motion capture and US imaging [21]. Achilles tendon length was defined as the distance between the gastrocnemius muscle tendon junction and the tendon insertion at the calcaneus. Panoramic ultrasound imaging allows the transducer to be moved along the patients Achilles tendon, blending multiple images together to form one long image with an extremely wide field of view [19]. The method is easy to perform and clinically applicable, but it has not been validated

[30][18][26]. Finally, Amlang et al reported an US classification system to be used for individual treatment selection in patients with ATR, looking at the degree of overlap of the torn tendon ends as a surrogate for tendon displacement and elongation [1]. This classification system is yet to be validated and correlated to the final outcome of treatment.

Magnetic Resonance Imaging (MRI) is also a non-invasive modality for tendon length measurement. Relative to US the setup is more demanding and expensive, as radiological assistance is needed to perform MRI measurements. Clinically, Matles test is the most widely used test for Achilles tendon elongation [12].

The purpose of the present study was to develop and validate a method, which can determine Achilles tendon length and elongation accurately in a clinical setting using standard US equipment. In order to do so we had the following specific aims: 1) US identification of the anatomical landmarks and development of the specific measurement. 2) Assessment of the intra-rater reliability and 3) of the inter-rater reliability. 4) Comparison of different modalities (Ultrasonography and MRI). 5) Comparison of the tendon length of both legs of the same subject.

MATERIAL AND METHODS

Description of the novel US measurement

Achilles tendon length was defined as the distance between the tendon insertion at the calcaneus and the medial gastrocnemius muscle tendon junction, as previously described by Rees et al. [21]. First, the anatomical landmarks were identified and marked, and then the distance between them was measured. The distal landmark was the posterior and most superior corner of the calcaneus in the midline, which on sagittal US examination was identified as the point where the cortical bone and its underlying shadow ended (figure 1). The proximal landmark was the distal tip of the medial gastrocnemius head, which was defined as the most distal point where the muscular fibers inserted into the v-shaped convergence of the deep crural fascia (figure 2).

Study population

Nineteen non-injured subjects, age 26 to 63 years, without prior Achilles tendon problems were included. Investigations were performed in the period November 2012 – January 2013. The study was approved by the Regional Ethical Review Board (Ref.No: SJ-318). All participants received oral and written information and written consent was obtained.

Setup

The novel US measurement was validated by three independent US-investigators with two to five years of experience within musculoskeletal US. MR-images were evaluated by two independent investigators, both specialized in musculoskeletal MRI. All investigators were blinded to the results of the other investigators and to their own previous results.

Inter- and intra-rater reliability for the novel US measurement was determined for the three independent US investigators on two occasions with three weeks between scans. Within the following two months MRI examinations were performed.

Participants were positioned in a prone position with the knee flexed 10 degrees. Anteriorly to (below) the ankle joint a triangle shaped foam pad was placed with the feet resting relaxed against it (figure 3). Using a goniometer the ankle joint was positioned in 10 degrees of plantar flexion by adjustment of the foam pad. Participants were positioned identically for US and MRI investigations.

Reliability-testing of the US measurement was performed using three different US scanners: GE Healthcare Logiq S8, Logiq 9 and logiq P5. Frequency was set to 15 MHz and focus was dynamically adjusted by the US operator. The predefined anatomical landmarks were identified using longitudinal imaging. A needle was placed between the probe and the surface of the skin, and the posterior acoustic shadow created by the needle on the US image was centered over the landmark. The position of the needle, thus representing the landmark, was then marked on the skin. (figure 3). The direct distance between landmarks was measured with a tape measure following the curves of the leg (figure 3). After each scan the marks on the skin were removed in order to secure blinding of results between investigators.

MRI setup

MR imaging was performed on a 1,5T system (Magnetom Avanto, Siemens, Erlangen, Germany). Axial 2D sequences covering both entire lower legs were performed as follows: T1 weighted without fat saturation (TR/TE, 485/12 ms; flip angle, 90°; pixel matrix, 384 x 256; voxel size, 1.2 x 0.9 x 6.0mm; slice thickness, 6.0mm; distance factor, 30%; FOV, 350 x 312mm; slices, 58), and T2 weighted without fat saturation (TR/TE, 4090/78ms; flip angle, 150°; pixel matrix, 448 x 355; voxel size, 1.0 x 0.8 x 6.0mm; slice thickness, 6.0mm; distance factor, 20%; FOV, 370 x 367mm; slices, 60). Sagittal 2D sequences covering each entire lower leg separately were performed as follows: T1 weighted without fat saturation (TR/TE, 555/22ms; flip angle, 180°; pixel matrix, 448 x 238; voxel size, 1.2 x 0.9 x 3.0mm; slice thickness, 3.0mm; distance factor, 10%; FOV, 410 x 291mm; slices, 37) and T2 weighted without fat saturation (TR/TE, 4740/72ms; flip angle,

150°; pixel matrix, 512 x 512; voxel size, 1.7 x 1.7 x 4.0mm; slice thickness, 4.0mm; distance factor, 20%; FOV, 440 x 440mm; slices, 26).

T1 weighted slices were used for all measurements. Length measures were performed from the most distal part of the medial head of the gastrocnemius muscle to the distal end of the Achilles tendon, which was defined by the axial plane intersecting the most cranial aspect of the tuber calcanei. Measurement was performed as follows: The measuring cursor was placed at the distal end of the Achilles tendon on the sagittal T1 slice. Keeping the cursor in this exact position the radiologist scrolled to the sagittal slice showing the most distal end of the medial head of the gastrocnemius muscle. The distance was then measured on this slice. The number of sagittal slices between the two measurement points was recorded and multiplied by the slice thickness (3.3 mm) to obtain the lateral distance between the two measurement points in the coronal plane. An estimate of the real length of the tendon was then calculated based on the craniocaudal measurement on the sagittal slice, and the lateralization estimate, using the equation of Pythagoras.

Statistical methods

The sample size was determined a priori after consultation with a biostatistician. The study was sized as an exploratory study. Standard procedures were used for descriptive statistics. Data were evaluated using the Bland-Altman method [2][3]. Difference of the mean and standard error of the measurement (SEM = SD x √(1 – ICC)) were calculated to assess the agreement between groups of data [29]. Limits of agreement and minimal detectable change (MDC) were calculated to assess agreement between data of the individual patients (MDC = 1.96 x √2 x SEM) [29]. Also the Inter correlation coefficient (ICC) was calculated. A paired t-test was used for comparison of means as the data showed a normal distribution and the scale was considered to be continuous. Statistical analysis where performed using the Statistical Package for Social Sciences (SPSS, version 20.0 for Windows, SPSS Inc, Chicago, III).

RESULTS

Both legs of 19 uninjured persons (8 males and 11 females) were studied. Their mean age was 43.4 years (SD 10.7, range 26-63). Average height was 175cm (SD 9, range 158-192) and average weight was 76.8kg (SD 12.9, range 58-110). They all had right as their dominant side.

Reliability

The novel US measurement showed excellent intra-rater reliability (ICC 0.96, SEM 0.37 and MDC 1.03) and inter-rater reliability (ICC 0.97, SEM 0.33 and MDC 0.93) (table 1). There was no systematic difference

between test days, but a systematic difference between investigators of 2.1mm to 4.5mm (P = 0.04 - <0.01). The variation of the inter-rater reliability measurements is shown in figure 4.
The MRI measurements showed an intra-rater reliability (ICC 0.99, SEM 0.16 and MDC 0.43) and inter-rater reliability (ICC 0.98, SEM 0.23 and MDC 0.64). There was no systematic difference between evaluations by the same investigator but a systematic difference between investigators of 3.5mm (P < 0.01). The variation of the inter-rater reliability measurements is shown in figure 5.

Validity

Validity of the novel US measurement was tested by comparison with the MRI measurements. The MRI measurements were on average 3.8mm longer than the novel US measurement (p=0.001); ICC 0.98, SEM 2.7mm and MDC 7.6mm. The variation of measurements is shown in figure 6. The average length of the measured Achilles tendons was 183mm; giving a measurement error of 3.8/183 = 2%.

Comparison of tendon length of the two legs

We found no statistically significant difference in length between the left and the right Achilles tendon assessed with both MRI and US. US measurements: p=0.95; ICC 0.94, SEM 4.1mm and MDC 11.5mm. MRI measurements: p=0.50; ICC 0.93, SEM 0.46mm and MDC 1.3mm. The variation of tendon length is shown in figure 7.

DISCUSSION

Elongation of the Achilles tendon after acute rupture is associated with inferior functional outcome [9][13][16][24]. The purpose of this study was to develop and validate a clinically applicable, accurate and easy to perform method for determining Achilles tendon length.

Measurement of tendon elongation in the acute and early phase of ATR is complicated by several factors. Firstly, anatomical landmarks are blurred due to rupture morphology. According to our experience the torn tendon ends consist of irregular fiber bundles of varying size and length. Therefore the diastasis between individual tendon fibers of the two ruptured ends may vary several centimeters. As such the actual displacement of the tendon ends cannot be measured by looking at the gap. Also, the distal insertion of the Soleus muscle-tendon junction is blurred due to hematoma. Secondly, when the tendon is ruptured, the position of the proximal end of the Achilles tendon varies with knee flexion and contraction of the Triceps surae muscle, and the position of the distal end of the Achilles tendon varies with the position of the ankle joint [23][20]. And finally, in order to measure elongation a reference value is needed. Although the length

of the right and left Achilles tendons previously have been shown to be equal, this finding is based on a small series, and further investigation is needed to confirm this [18].

The existing methods used to measure Achilles tendon length and elongation are not applicable in the acute and early phase following ATR. RSA allows for very accurate measurements, but the technique is not applicable as a clinical tool, as it measures displacement of the torn tendon ends in the period after application of the markers and not the actual displacement in the acute phase, and thus tendon elongation. The invasive nature of the technique also disqualifies it for evaluation of non-operative treatment of ATR. US imaging combined with video-based motion capture also allows for accurate and valid measurements: Accuracy (<1% error) and reliability (ICC=0.97; SEM=0.4cm; MDC=1.1cm) [24]. However, the method is not applicable as a diagnostic tool in clinical work due to its complicated setup. Panoramic US imaging appeared to be a promising method. Unfortunately it showed an unacceptable intra- and inter-rater reliability in an unpublished pilot study performed on the same study population with same study setup (ICC=0.84; SEM=0.9cm; MDC=2.6cm). MRI measurements are non-invasive and accurate but time consuming and expensive to perform [5]. Moreover, the expense of advanced imaging modalities such as MRI must be justified in the light of rapidly rising health care costs [28]. Clinically, Matles test is the most widely used test for Achilles tendon elongation [12]. The test is easy to perform and can easily be applied intra-operatively. It does, however, not give an exact value but a rough estimation of elongation; and despite its use for many years, it is still to be validated and correlated with the final outcome of treatment.

The relationship between Achilles tendon elongation and functional deficit needs to be further investigated. An average elongation after ATR of 2.5-3.5cm has been found in small series of patients, and a linear relationship between deficits in heel-rise-height and tendon elongation has been proposed [24][27]. However, the acceptable Achilles tendon elongation after rupture still needs to be clarified.

In the present study, US- and MRI measurement both showed excellent reliability (table 1, figure 4 and 5). For comparison between groups of non-injured subjects, differences in length of Achilles tendons of more than 4mm and 2 mm can be detected with the US and MRI measurements respectively. For repeated assessment of individual subjects differences in length of Achilles tendons of more than 10mm and 6 mm can be detected with the US and MRI measurements respectively. Accuracy of the novel US measurement was considered acceptable (error 2%). A certain difference between measurements was expected, as the anatomical landmarks appear different on US and MR imaging. It is not within the scope of this study to determine which of the two measurements is the most accurate. The reliability and validity of the novel US

measurement is comparable with the method combining video-based motion capture and US imaging [21][24]. Roentgen Stereophotogrammetric Analysis is far more precise (0.01mm – 0.025mm), but does not measure the actual tendon length and it is not clinically applicable [11].

When assessing elongation of a ruptured Achilles tendon, a reference value is needed. The healthy leg being the obvious choice, we measured the difference in length between the right and the left side, as previously described by Pang and Ying [18]. We found no systematic difference in length of the two Achilles tendons, but a rather large variation (table 1 and figure 7). Due to this variation in length of the two Achilles tendons an additional error was introduced in all measurements using the uninjured side as reference. Looking at groups of patients an error of 5mm is introduced when using the uninjured side as reference, and for repeated assessment of individual subjects an error of 13mm is introduced when using the uninjured side as reference. It should also be noted that this study investigated non-injured subjects and that data not necessarily can be directly applied in an injured population.

The novel US measurement is a promising clinical tool. It is accurate, reproducible, cost-effective, easy to perform and non-invasive. However, it needs to be evaluated in a population with acute Achilles tendon rupture. The next obvious point of research is the correlation between 1) tendon elongation in the acute and early phase of rupture and 2) the length and functional result after rehabilitation. Moreover, if tendon elongation in the acute and early phase of rupture does in fact correlate with inferior clinical function the novel US measurement might allow for individualized and optimized treatment of ATR.

Conclusion

The novel US measurement showed good reliability and accuracy. For comparison between groups of non-injured subjects differences of more than 4mm can be detected. For repeated assessment of individual subjects differences of more than 10mm can be detected. The novel US measurement is a promising clinical tool to be further assessed in the setting of acute Achilles tendon rupture.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

TABLES

Table 1: Results

	ICC	SD crude (cm)	SEM (cm)	MDC (cm)	Diff. mean (cm)	P-value	Upper LoA (cm)	Lower LoA (cm)
Reliability: The novel US measurement								
Intra-rater reliability	0.96	1.86	0.37	1.03	-0.097	0.18	1.35	-1.55
Inter-rater reliability (1-2)	0.97	1.81	0.33	0.93	-0.21	0.04	1.43	-1.85
Inter-rater reliability (1-3)					0.24	0.02	1.99	-1.51
Inter-rater reliability (2-3)					0.45	<0.01	1.87	-0.97
Reliability: MRI measurements								
Intra-rater reliability	0.99	1.74	0.16	0.43	0.056	0.14	0.66	-0.55
Inter-rater reliability	0.98	1.76	0.23	0.64	0.35	<0.01	1.26	-0.57
Validity: US measurements compared with MRI measurements								
US - MRI	0.98	1.77	0.27	0.76	0.38	<0.01	1.47	-0.71
Comparison of tendon length of the two legs								
right - left	0,93	1,76	0,46	1,26	-0.15	0.95	1.63	-1.92

LEGEND: ICC: Inter Correlation Coefficient; SD crude: Standard deviation of the crude measurements; SEM: Standard error of measurement; MDC Minimal Detectable Change; Diff.mean: Difference of the mean; P-value: Significance level of the Diff.mean; Upper LoA: Upper Limit of Agreement (diff.mean + 2 standard deviations); Lower LoA: Lower Limit of Agreement (diff.mean - 2 standard deviations). Intra-rater reliability of the novel US Measurement was tested by three investigators. The Bland-Altman method only allows for comparison of two investigators; thus results are shown for the three pairs of investigators (1-2, 1-3 and 2-3).

FIGURES

Figure 1: A sagittal US picture showing the insertion of the Achilles tendon at the calcaneus. The distal landmark, the posterior-superior corner of calcaneus, is seen as the point where the cortical bone and its underlying shadow ends. A 21 gauge needle is positioned between the probe and the skin without penetrating the skin. The landmark is projected to the skin by the posterior acoustic shadowing of the needle.

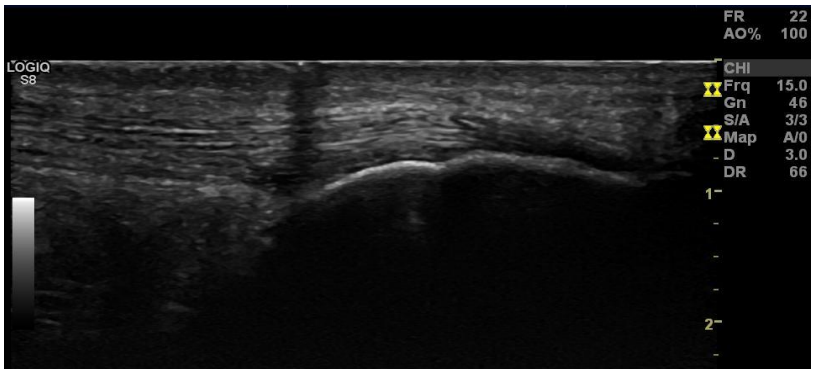


Figure 2: A sagital US picture showing the muscle-tendon junction. The proximal landmark is the distal tip of the medial gastrocnemius head (the insertion of the most distal muscle fibers into the deep fascia). A 21 gauge needle is positioned between the probe and the skin without penetrating the skin. The landmark is projected to the skin by the posterior acoustic shadowing of the needle.

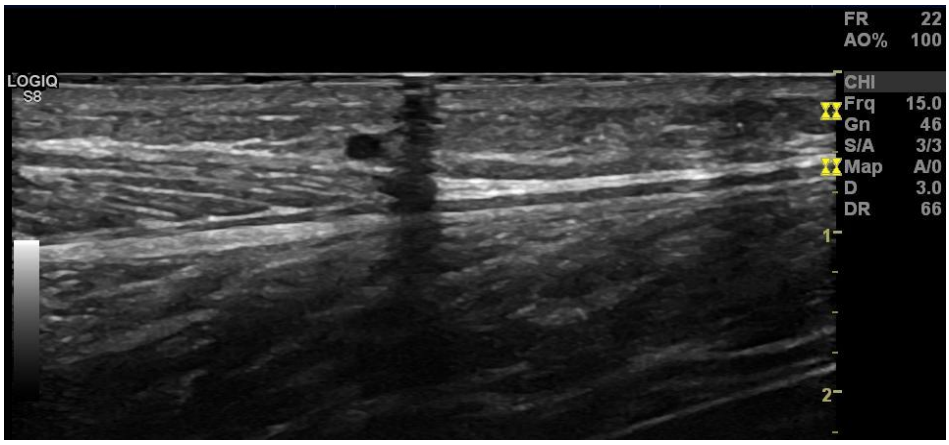


Figure 3: Positioning of the study subjects. Participants were positioned in a prone position with the knee flexed 10 – 20 degrees. The ankles rested on a triangular foam pad. Using a goniometer the ankle joint was positioned in 10 degrees of plantar flexion by adjustment of the foam pad (A). With a marker the point where the US probe and the needle crossed was marked on the skin (B+C). The distance between landmarks was measured with a tape measure following the curves of the leg (D).

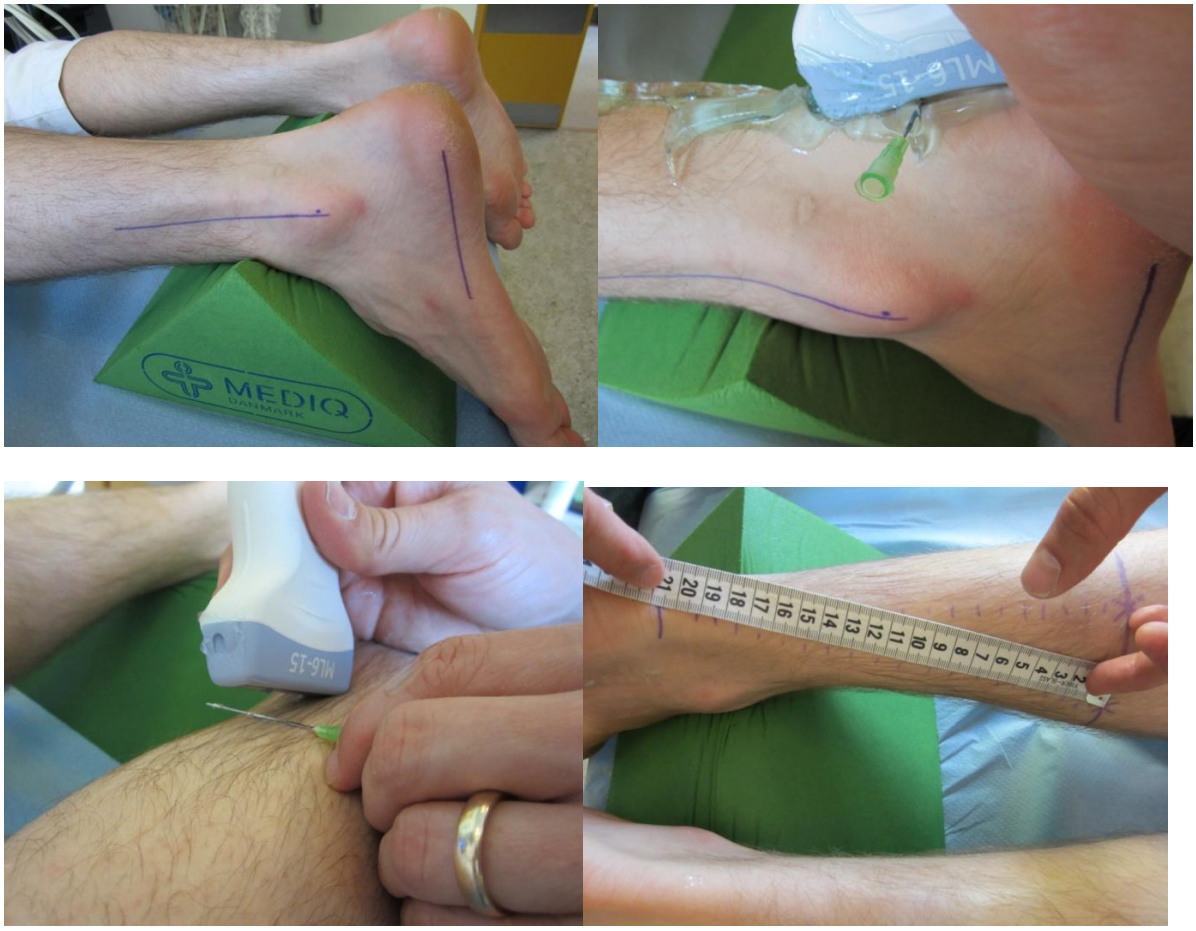


Figure 4: Inter-rater reliability of the novel US measurement. Bland Altman Plot showing difference against mean. Measurements are shown in cm.

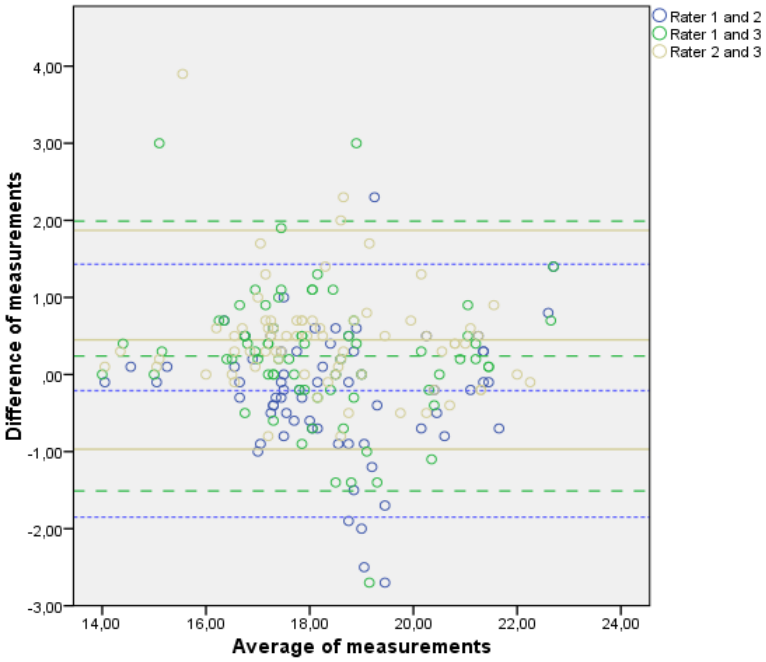


Figure 5: Inter-rater reliability of the MRI measurement. Bland Altman Plot showing difference against mean. Measurements are shown in cm.

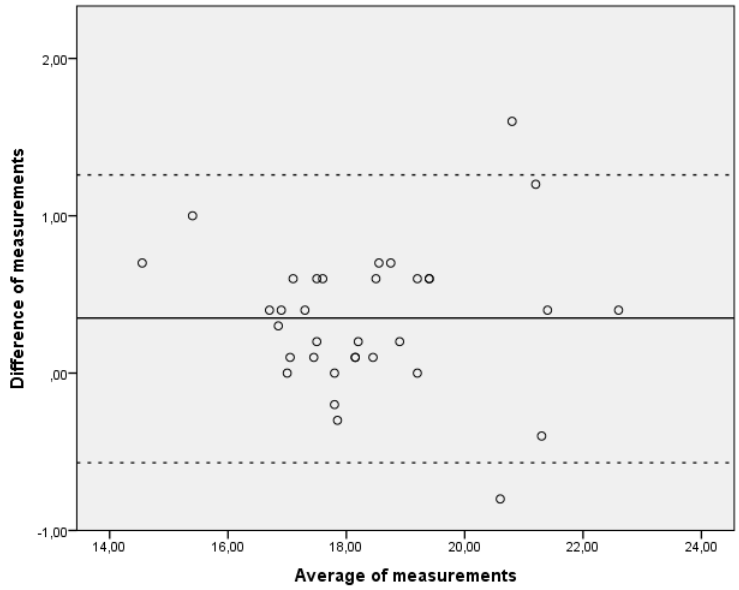


Figure 6: Difference of US and MRI measurements. Bland Altman Plot showing difference against mean. Measurements are shown in cm.

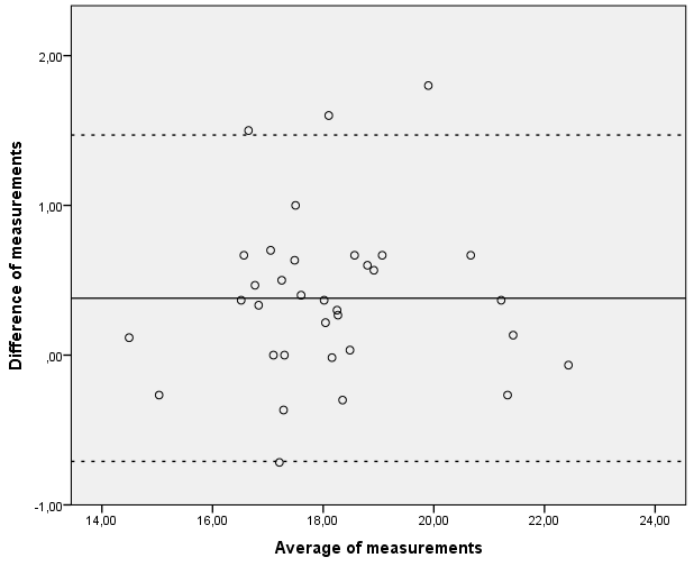
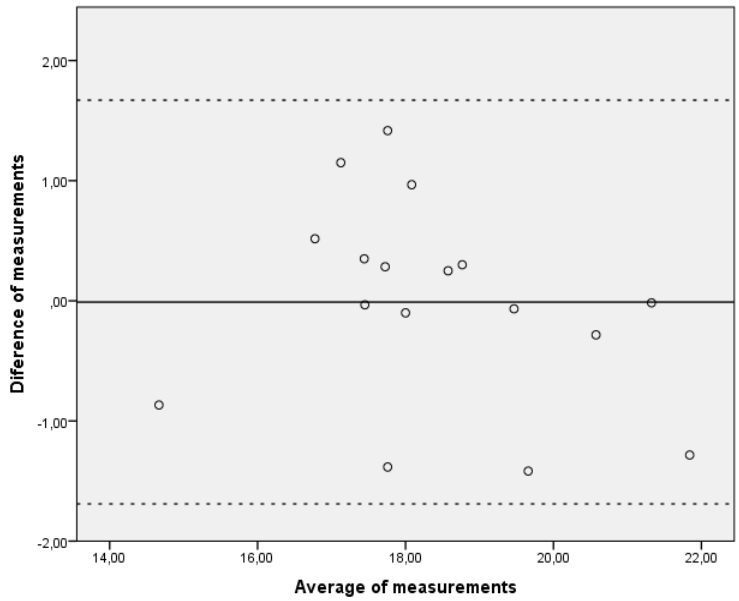


Figure 7: Difference in tendon length between the left and right leg. Bland Altman Plot showing difference against mean. Measurements are shown in cm.



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