TIMO NYYSSÖNEN

Achilles tendon rupture
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Author’s address: Department of Orthopaedics, Traumatology and Hand Surgery, Kuopio University Hospital
University of Eastern Finland
KUOPIO
FINLAND

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Supervisors: Docent Peter Lüthje, M.D., Ph.D.
University of Helsinki
HELSINKI
FINLAND

Professor Heikki Kröger M.D. Ph.D.
Department of Orthopaedics, Traumatology and Hand surgery, Faculty of health Sciences
University of Eastern Finland
KUOPIO
FINLAND

Reviewers: Assistant Professor Ville Mattila, M.D, Ph.D.
Department of Orthopaedics and Traumatology
University of Tampere
TAMPERE
FINLAND

Docent Jari Parkkari, M.D, Ph.D.
UKK institute - Research Center of Sports Medicine
University of Tampere
TAMPERE
FINLAND

Opponent: Professor Juhana Leppilahti, M.D., Ph.D.
Department of Orthopaedics and Traumatology
Oulu University Hospital
OULU
FINLAND
ABSTRACT

The first factual descriptions of Achilles tendon trauma originated in ancient Greece. The incidence of Achilles tendon rupture in industrialized countries has increased during recent decades. The reasons for this increase are largely unknown. Even today, the treatment of Achilles tendon rupture is debated. There are variations in the indications for operative treatment, and the results of the surgical treatment are inconsistently reported.

The aim of this doctoral thesis was to examine the results of the treatment, to investigate the epidemiology at the national level and to determine predisposing factors associating Achilles tendon rupture to medical drug treatments, if any. The first part of study investigated the injury mechanism, the results of the treatment and the typical complications based on retrospective data (I). The next part compared two operative methods, end-to-end suturing and suturing reinforced with a tendon flap (II). The third part of study investigated the incidence, age and sex of 7375 patients with Achilles tendon rupture from 1987-1999 using a national registry (III). Finally, the association of Achilles tendon rupture with medical drug treatments during the year preceding the injury was examined in a matched cohort study (IV).

Major complications after Achilles tendon repair are rare. However, operative treatment is currently indicated in selected patients only. Tendon reconstruction reinforced with gastrocnemial aponeurosis flap compared to simple tendon suturing has more local soft tissue related complications. Therefore, simple tendon suturing should be appropriate, at least in uncomplicated acute ruptures. The incidence of Achilles tendon rupture significantly increased between years 1987-1999 in Finland. The injury was more common in men, and the mean age of the patients was 42 years. Several medical drug treatments, including fluoroquinolone antibiotics, are associated with Achilles tendon rupture. The statistically significant association with renin-angiotensin II receptor antagonists was previously unreported.
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TIIVISTELMÄ


Yleinen suomalainen ontologia: kantajänne, vammat, esiintyvyys, riskitekijät, hoitotulokset
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Everything started in 1998. As a young resident surgeon, I was asked to determine the results of Achilles tendon rupture treatment in a small hospital in South-East Finland. The report was successfully published, and ever since, the study has expanded. Over time, methods have evolved, from descriptive statistics to matched cohort studies. In addition to scientific objectives, this is a story of a growing orthopaedic surgeon. During the many silent years, scientific intentions gave way to a clinical career. Now, at last, it is time to finalize the slowly evolved study on Achilles tendon rupture.

I am very grateful to Dr Peter Lüthje. He is the genuine primus motor behind this project. During the long years, in fact two decades, he has continuously encouraged me. Without his patient and reliable support, I would probably have given up a long time ago.

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Finally, I want to thank my family. My wife Mari has proofread my articles with excellent knowledge in English grammar, and my children Juuso, Iina and Aaro have provided technical help in editing the text. The next generation has sharp minds and fast fingers.

Kuopio, September 2020
Timo Nyyssönen
LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications:


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Start by doing what’s necessary, then what’s possible and suddenly you are doing the impossible.
ABBREVIATIONS

AOFAS  American Orthopaedic Foot and Ankle Society hind-foot score
AT    Achilles tendon
ATRS  Achilles tendon total rupture score
BMI   Body mass index
CT    Computer tomography
DVT   Deep vein thrombosis
MRI   Magnetic resonance imaging
NHII  National Health Insurance Institution
PE    Pulmonary embolism
RAS   Renin-angiotensin receptor antagonists
RAS-2 Renin-angiotensin II receptor antagonist
RCT   Randomized controlled trial
ROM   Range of movement
SF-36 Short Form (36) Health Survey
Statins  HMG CoA reductase inhibitors
UEF   University of Eastern Finland
US    Ultrasound
1 INTRODUCTION

The name of the Achilles tendon (AT) originates from Homer’s Iliad poem in ancient Greece. The structure of the strong posterior leg tendon results from the upright position of humankind and a functional AT is essential for normal gait. The first closed rupture was described by Ambroise Pare in the 16th century and the first open repair was documented in 1888 by French Polaillon (Kleenerman et al. 2007).

AT rupture results in loss of ankle plantar flexion force and the main priority of treatment is to restore normal heel-raise function. Conservative treatment involves temporary immobilization of the ankle in plantar flexed position for a few weeks before it is changed to neutral position. Nowadays early mobilization and weight-bearing have been widely preferred (Gross and Nunley 2016). There are many operative techniques for AT rupture, both open and percutaneous mini-invasive surgery (Webb and Bannister 1999, Deng et al. 2017, Ochen et al. 2019). According to recent literature operative surgical treatment is associated with a low risk for recurrent rupture and, to some extent, better functional results compared to conservative treatment (Ochen et al. 2019). However, patients receiving operative treatment are prone to deep infections which are frequently challenging to treat. Poorly standardized clinical scores and measurements have complicated the evaluation of outcomes. Optimal treatment for AT rupture remains controversial, although operative treatment is generally preferred for athletes.

The number of AT ruptures has been increasing (Huttunen et al. 2014, Lantto et al. 2015b, Mattila et al. 2015, Sheth et al. 2017). The reasons for this trend are controversial and probably multifactorial. As well, the median age of the patients has been increasing (Ho et al. 2017). Most AT ruptures are sports-related (Scott et al. 2014); therefore, changes in sporting habits and lifestyle in addition to improved diagnostics in industrialized countries have been suggested as probable causes for the increase. The risk for AT rupture is increased in certain medical conditions. According to the literature, patients with hyperparathyroidism, rheumatoid disease, familial hypercholesterolemia and renal transplant are predisposed to AT rupture (Ames et al. 2008). Some medications have adverse tendon effects. There are multiple reports about fluoroquinolone-induced AT tendinopathy (Stephenson et al. 2013). Moreover, AT tendinopathy has been associated with the long-term use of glucocorticoids and aromatase inhibitors. An increased risk for AT rupture has recently been suspected among patients using statin treatments (Kirchgesner et al. 2014, Teichtahl et al. 2016).

This thesis includes four studies each with distinct data and objectives. The main purpose of this project was to explore the results of treatment, to investigate the epidemiology at the national level and to determine predisposing factors that affect the risk of AT rupture associated with medical drug treatments, if any are found.
2 REVIEW OF THE LITERATURE

2.1 ACHILLES TENDON ANATOMY AND FUNCTION

The Achilles tendon is a very strong 12 - 15 cm long fibrous structure that connects the main muscles of the leg’s superficial posterior compartment to the calcaneal bone. The gastrocnemius and soleus muscles have different proximal origins but share a conjoined distal part known as the AT. The third muscle of the posterior compartment, the plantaris muscle, has its own weak tendon. The AT proximal tendomuscular junction is flat and broad, whereas the middle part of the tendon is round. The tendon insertion in the calcaneal bone’s posterior margin is crescent shaped and has significant medial and lateral projections. (O’Brien 2005)

The AT is surrounded by a thin connective tissue sheath, called a peritenon, which provides tendons with a gliding surface and transmits blood supply. The vascular supply for the middle part of the tendon is supplied by the peroneal artery, and the proximal and distal sections are supplied by the posterior tibial artery. The vascular supply to the AT is weakest in the middle area 2-6 cm from the calcaneal insertion point. The origin and insertion points have more abundant vascularization. The local blood supply for the AT varies according to age (Doral et al. 2010). The AT derives its innervation from the sural nerve with a smaller supply from the tibial nerve.

The main part of the tendon consists of longitudinal fascicles. The fascicles enclose multiple collagen fibrils, which provide the tendon with a strong axial load capacity. Spiralization of the tendon fibres produces an area of concentrated stress and confers a mechanical advantage. The AT contains many types of collagen, but the most common is longitudinally oriented type I. Collagen fibres make up to 90% of the tendon protein content. The cells maintaining the structure are 90-95% tenocytes and tenoblasts. The extracellular matrix is highly hydrophilic, which promotes elastic properties. (Hong-Yun et al. 2016)

The AT is the main plantar flexor of the ankle. Evolutionally, the tendon has adapted to an upright position and allows humans to jump and run efficiently. In addition, it is a spring and shock absorber during gait (Malvankar and Khan 2011). Due to its proximal insertion to the femoral condyles, the gastrocnemius muscle function is maximal when the knee joint is extended. In contrast, soleus muscle function is independent of knee position (Doral et al. 2010). The AT is the most frequently ruptured tendon in the human body, even though it is the strongest. The pullout strength of healthy ATs in cadaver tests has been reported to be $1300 \pm 500$ N (Pfeffer et al. 2018), but direct measurements of forces have revealed peak loading as high as 9 KN during running.
Fig.1. Normal Achilles tendon exposed in cadaver model. Suralis nerve (*) passing oblique from medial to lateral aspect of the tendon is prepared. The calcaneal bone is covered by distal tendon insertion. The narrowest part of the tendon, 2-6 cm proximal from the insertion, is a frequent position for an AT rupture.

2.2 AETIOLOGY OF ACHILLES TENDON RUPTURE

Sometimes the AT might rupture suddenly with only minor ankle distension injury. The tendon is vulnerable to incisive forces, but the great majority of the ruptures are closed. Frequently, there are clear predisposing degenerative histopathological changes, even without notable signs or symptoms (Järvinen et al. 2005). Supposedly, the degenerative process and the tendon tears are part of a continuum that starts with a partial-thickness tear and subsequently leads to a full-thickness rupture. The reason for the apparent weakening of the AT before rupture is controversial and involves biological, anatomical, and mechanical factors.
2.2.1 Preceding tendinopathic changes

AT tendinopathy is a common degenerative condition characterized by local pain, swelling and impaired performance. The diagnosis is mainly based on a patient’s history and clinical examination. The acute inflammation of the AT, tendinitis, should be dissociated from chronic tendinopathy. The aetiology of AT tendinopathy is unknown. Tendon vascularity, gastrocnemius-soleus dysfunction, age, sex, body weight and height, pes cavus, and lateral ankle instability are considered common intrinsic factors (Longo et al. 2018).

Anatomically, AT tendinopathy is classified into insertional and non-insertional variants. The more common insertional tendinopathy is associated with old age, obesity, diabetes and inflammatory arthropathies (DeOrio and Easley 2008). Degenerative changes in insertional tendinopathy are evidently located at the calcaneal insertion point, and frequent symptoms are pain in the morning. The insertion site of the AT might be calcified and the calcaneal tuberosity prominent, which is named Haglund’s’s deformity (DeOrio and Easley 2008). On the contrary, lesions in non-insertional tendinopathy occur between 2 and 6 cm from the distal insertion point (Roche and Calder 2013). This is the area of relatively weak vascular supply and a frequent site of AT rupture (Doral et al. 2010). Both partial and total AT ruptures have been associated with non-insertional tendinopathic lesions. A partial rupture has been found in 23% of tendons operated on for non-insertional tendinopathy (Åström 1998).

Histopathological examinations of pathological tendons constantly demonstrate proliferation of tenocytes, altered collagen fibres and a subsequent increase in non-collagenous matrix (Longo et al. 2018). The pathological tendon cells produce relatively more type III collagen, which may affect the tensile strength. The increased rate of matrix remodelling leads to a mechanically less stable tendon, which is more susceptible to rupture. These changes are generally considered a failed healing response (Li and Hua 2016). At the end-stage of the degenerative process, fibrosis and calcification of the peritendinous tissue might emerge. Finally, the degenerative changes naturally increase with age.

According to the literature, neovascularization is a common discovery in Doppler sonography of tendinopathic tendons. However, 16% of symptomless young people have abnormal AT sonography findings (Noback et al. 2018). The association of neovascular lesions and painful symptoms is contradictory (De Marchi et al. 2018). Hypervascular tendon lesions have been treated by injections of a sclerosing agent; nevertheless, in a recent RCT, the mid-term results were equal to placebo treatment (Ebbesen et al. 2018).
2.2.2 Tendon injury mechanism

McMaster proposed almost 90 years ago that a healthy tendon never ruptures (McMaster 1933). However, overwhelming axial traction of healthy AT results in equal risk for corruption in central part of the tendon, muscle- and bone- insertion. The risk for tendon rupture is particularly high with oblique force (Barfred 1971). Many sports require rapid accelerations and changes of direction. This motion results in rotation of the calcaneal bone concurrently with a maximal muscle contraction, which predisposes patients to AT rupture.

AT rupture might be a consequence of excessive and repetitive mechanical loading. Tendon cells are mechanosensitive; they alter their extracellular matrix in response to local loading demands. Continuous overload results in dysfunction, which is characterized by improper collagen fibril diameter formation, collagen fibril distribution and overall fibril misalignment (Galloway et al. 2013). Failed healing responses have been categorized into three successive stages: immediate reactive tendinopathy, tendon disrepair and degenerative tendinopathy (Li and Hua 2016). Consequently, multiple microtraumas could expose an AT to risk of a complete rupture.

According to microvascular measurements, physical activity increases temporary blood flow to the AT. This reaction is significantly lower in the older population than in the younger population. Furthermore, males have a lower increase than females in blood flow (Wezenbeek et al. 2018). The highest incidence of AT ruptures has been reported in middle-aged recreational male athletes.

Certain preceding conditions increase the risk for AT rupture. A preliminary period of ischiatic pain (Maffulli et al. 1998) and a history of ankle sprain (Fulton et al. 2014) have been associated with AT rupture. It is possible that malfunctions in the proprioceptive component of skeletal muscle exposes patients to tendon rupture.

Many people engaged in recreational sports have AT tendinopathy, which predisposes them to rupture. Factors related to tendinopathy include inadequate stretching, training errors, mechanical malalignment of the lower extremities and certain training surfaces (Galloway et al. 1992). AT tendinopathy is the most common overuse injury in master running athletes. Running on soft surfaces increases the risk of mid-portion AT tendinopathy compared to those who run on hard surfaces (Knobloch et al. 2008). The risk for mid-portion tendinopathy is increased in runners with over-pronation of the hindfoot during the mid-stance of the running gait (Ryan et al. 2009). Excessive pronation decreases the local blood flow in the AT (Wezenbeek et al. 2017). Although abnormal lower limb biomechanics have been speculated to be a risk factor for AT rupture, these findings need to be interpreted with caution without a well-designed prospective study (Munteanu and Barton 2011). The treatment of overuse injuries is initially conservative, including passive stretching and strengthening exercises. The training errors and erratic limb alignment should be corrected (Galloway et al. 1992).
2.2.3 Systemic predisposing factors

Multiple systemic medical conditions have tendon effects. Patients with familial hypercholesterolemia, rheumatoid disease, hyperparathyroidism and renal transplantation are predisposed to tendinopathy (Ames et al. 2008, Humbyrd et al. 2018). In addition, there are sporadic case reports of AT ruptures with rare inflammatory and autoimmune diseases, genetically inherited collagen abnormalities, infectious diseases and neurological conditions. On the other hand, smokers and patients with cardiac disease have a lower incidence of AT tendinopathy than healthy subjects, which might be explained by lifestyle factors. According to a matched pair analysis, there is no statistically significant hereditary risk for AT rupture (Kraemer et al. 2012).

According to the literature, systemic or local administration of several drugs might cause alterations in tendons. Toxic tendinopathy has been reported in association with four drug classes: fluoroquinolone antibiotics, glucocorticoids, statins and aromatase inhibitors. Frequently, the AT is affected. Additionally, there are sporadic case reports of tendinopathy with metalloproteinase inhibitors, isotretinoin, anabolic steroids and antiretroviral agents. (Bolon 2017)

Fluoroquinolone antibiotics are associated with tendon disorders. According to a recent meta-analysis, patients receiving fluoroquinolone treatment had a risk with an odds ratio of 2.52 for AT rupture (Alves et al. 2019). The risk has been found to be particularly high with concomitant old age and exposure to oral corticosteroids (Morales et al. 2019). There is evidence of a direct effect on tendon cells in animal models. Fluoroquinolones have resulted in large cytoplasmic vesicles in tenocytes and general disruption of the extracellular collagen matrix. The changes are dose dependent (Szarfman et al. 1995, Shakibaei et al. 2000). There are numerous reports of bilateral AT ruptures associated with fluoroquinolone treatment (Kawtharani et al. 2016). Tendon rupture might emerge a few days after medical drug treatment (Bolon et al. 2017). Patients with signs of tendinopathy should be recommended to discontinue the treatment and rest until the symptoms have resolved.

Corticosteroid injection therapies have been used for Achilles tendinopathy and retrocalcaneal bursitis, even though the evidence for the treatment is negligible. (Metcalfe et al. 2009, Gross et al. 2013). Multiple case reports indicate short-term pain relief, which might mask the symptoms and predispose patients who maintain a high level of physical activity to AT rupture. An injection of hydrocortisone in rabbit AT causes local necrosis in 45 minutes (Hugate et al. 2004). According to Cochrane database the evidence for AT injection therapies is insufficient (Kearney et al. 2015).

Oral corticosteroids have been used for a long time in the treatment of chronic obstructive airway disease. According to case reports, long-term use of systemic corticosteroids might be associated with AT rupture (Newnham et al. 1991). The rupture risk has been verified in a case-control study (Spoendlin et al. 2015). In the study, the odds ratio was 3.0 for AT rupture and oral corticosteroids, whereas inhaled corticosteroids had no effect. Histopathological studies of systemic corticosteroid administration in rats have shown immature collagen fibres and decreased tendon
strength (Taguchi et al. 2016). In contrast, corticosteroids given after the early inflammation phase have improved healing of AT rupture (Blomgran et al. 2017).

Statins are drugs used to treat hypercholesterolaemia. There are conflicting reports of the risk for AT rupture among patients using statins (Marie et al. 2008, Spoendlin et al. 2016). According to some authors, tendinopathy may occur within the first year of statin use and may improve after drug therapy is stopped (Marie et al. 2008, Deren et al. 2016, Bolon 2017). In contrast, no positive association was found in a systemic review (Teichtahl et al. 2016) or a recent cohort study with a 5-year follow-up time (Spoendlin et al. 2016). The pathogenesis of statins affecting the AT is incompletely understood. According to a report, rats treated with statins have thinner epitenons and decreased tendon strength due to altered organization of collagen fibres (De Oliveira et al. 2015). However, ultrasound examination of patients using statins for at least one year revealed no difference in tendon structure (de Sá et al. 2018).

Aromatase inhibitors are used to treat hormone-sensitive breast cancer in postmenopausal women and gynaecomastia in children and adolescents. Adverse tendon events associated with this drug are exceedingly rare, and only a few case reports have been published (Mitsimponas et al. 2018).

## 2.3 EPIDEMIOLOGY OF ACHILLES TENDON RUPTURE

### 2.3.1 Increasing incidence and age

The incidence of AT ruptures has increased in the industrialized world over the last 50 years (Raikin et al. 2013, Huttunen et al. 2014, Lantto et al. 2015b, Ganestam et al. 2016). The increasing trend has been verified in numerous reports. A nationwide study in Sweden reported an increase of 17% in men and 22% in women between years 2001 and 2012 (Huttunen et al. 2014). This study included not only operatively treated patients, but outpatients visits as well. AT rupture incidence has been studied in the Oulu region of Finland. The first study compared the time periods 1979 – 1986 and 1987 – 1994. The incidence increased from 2/10⁵ to 12/10⁵ (Leppilahti et al. 1996). The second study reported a statistically significant increase from 2.1/10⁵ in 1979 to 21.5/10⁵ in 2011 (Lantto et al. 2015b). According to the last-mentioned study, the incidence of non-sport-related ruptures increased steadily over a long time period, whereas sport-related ruptures increased more towards the end of the study period. In Finland the rate of operatively treated AT rupture patients has increased until years 2007 – 2008. Since then nonoperative treatment method has become more common (Mattila et al 2015). Regardless, research on the incidence of AT rupture has been conducted in industrialized Western countries only and might be limited to closed AT injuries. However, the great majority of AT ruptures are closed.

The average age at the time of AT injury has been reported to be 46 years in the USA (Raikin et al. 2013), 45 years in Denmark (Ganestam et al. 2016) and 39 years in Canada (Scott et al. 2014). There is a rising trend of the age of the patients over time.
A statistically significant increase between 1953 and 2014 has been reported in a literature review including demographics from 142 studies. The mean age increased over time by at least 0.721 years every five years (Ho et al. 2017). According to some authors, the increasing total number of AT ruptures is mostly based on increasing incidence in the older population (Ganestam et al. 2016). There are reports of two peaks in AT rupture age distribution, the first occurring in 30- to 39-year-olds and a second in older age (Möller et al. 1996, Maffulli et al. 1999). The bimodal age distribution is not verified in all studies. Patients older than 55 years of age are more likely to be injured in non-sport-related activities, and their diagnoses are more likely to be delayed more than 4 weeks following the injury (Raikin et al. 2013).

2.3.2 Sport-related injuries with possible seasonal variation

Most closed AT ruptures are sport related. Sporting activities have been reported to be responsible for 68% - 76% of ruptures in the USA and Canada. This statistic was even more prominent in patients younger than 55 years of age (Raikin et al. 2013, Scott et al. 2014). According to retrospective inquiry, patients with AT ruptures are more active in sports than patients with ankle sprains (Noback et al. 2017). Several authors have suggested that the increasing incidence of AT rupture is a result of the increasing popularity of certain sporting activities (Järvinen et al. 2005). A slight left leg predominance in AT ruptures has been reported (Jozsa et al. 1989).

Participation in specific sports, most commonly ball games, has been associated with an increased risk of AT rupture. There are regional and temporal differences in the frequency of sport activities. As a result, the sport most associated with AT rupture varies. According to reports, the most dangerous sports have been football in Germany (Winter et al. 1995), badminton in Denmark and Sweden (Wahlby 1978, Nillius et al. 1976) and volleyball in Finland (Leppilahti 1996). In the USA, AT ruptures most commonly occurred in basketball, followed by tennis and football, 32%, 9% and 9% respectively (Raikin et al. 2013). Generally, any sports involving repetitive heel rises, such as running, increases the risk. Long-distance runners have been reported to have a tenfold increase in AT injuries compared to age-matched controls (Rompe et al. 2008).

The cyclic nature of some sports activities might result in seasonal variation of AT ruptures. The studies considering seasonal variation have reported mixed results. According to a retrospective study in Canada, there was an increased number of sport-related injuries in spring. However, the non-sport-related cases were distributed evenly throughout the year (Scott et al. 2014). An epidemiologic study carried out in New York demonstrated the highest incidence in spring and the lowest incidence in fall, with statistically significant differences between seasons (Caldwell et al. 2018). Another study in Sweden reported significantly higher AT rupture incidence during winter and spring and lowest during summer (Saarensilta et al. 2020).
2.3.3 Sex, BMI and AT-rupture

The sex difference of the AT rupture rate is well known. Most patients are men, and the reported ratio varies from 2:1 to 19:1 (Zollinger et al. 1983, Carden et al. 1987, Scott et al. 2014). However, the relative proportion of female AT rupture patients has increased over time. According to a review article of publications in 1953 - 2014, the percentage of female patients increased by at least 0.6% every five years (Ho 2017). A similar trend has been reported in Sweden (Huttunen et al. 2014).

The incidence of lower extremity tendinopathies is higher in men. Reasons for this incidence are controversial, but differences in sport activities and hormonal factors have been suspected (Kjaer and Hansen 2008). There is no sex difference whether the injury is sport-related or not, but the average age at the time of injury might be sex related. A higher average age of affected females has been reported in Scotland and Canada (Maffulli et al. 1999, Suchak et al. 2005); on the other hand, more recent studies demonstrated that men were 1 – 2 years older at the time of injury than females (Scott et al. 2014, Ganestam et al. 2016).

The effect of body weight on AT rupture risk is controversial. The reported BMI of rupture patients is equivalent to that of the normal healthy population (Noback et al. 2017). However, there are some facts to consider. Patients with high BMI have more AT tendinopathic changes (Scott et al. 2013) and seem to have different tendon structures on ultrasound examination compared to the normal population (de Sá et al. 2018). In addition, patients with BMI greater than 30 are more likely to be injured in nonsporting activities and to have their diagnosis initially not recognized (Raikin et al. 2013). The relative proportion of AT rupture patients with high BMI has not changed significantly over time (Ho et al. 2017).

2.4 DIAGNOSIS

Acute total AT rupture is usually easy to diagnose clinically. Frequently, the patients have a history of trauma with immediate loss of ankle plantar flexion power. Instant pain and even a sudden audible snap at the time of injury are common. In the early stage, swelling and bruising might not be visible. Delay in treatment reportedly has detrimental effects on the final outcomes. Therefore, it is important to accurately diagnose an acute injury early. A retrospective review in the USA reported that only 76% of AT ruptures were diagnosed and managed in less than 4 weeks (Raikin et al. 2013). Partial ruptures are less obvious to evaluate, and delays in the diagnosis and treatment are common. The signs and symptoms of tendinopathy might hide a rupture. The other differential diagnoses for subacute AT ruptures are retrocalcaneal bursitis, os trigonum, tarsal tunnel syndrome, posterior tibialis tendon rupture, arthritic conditions, plantar fasciitis and stress fracture (Hutchison et al. 2013). In uncertain cases, additional investigations including plain radiographs, ultrasound or MRI can be performed to exclude any bony pathology or to confirm the diagnosis.
2.4.1 Physical examination

Simple clinical measures are readily accessible to clinicians. A comprehensive clinical examination incorporating such measures is suggested to outperform MRI with respect to diagnostic accuracy for Achilles tendon rupture (Garras et al. 2012). It is always recommended to test bilateral ATs for comparison. Many physical tests to diagnose AT rupture have been reported.

Frequently AT rupture patients have a gap in the AT, typically 3 - 6 cm above the insertion into calcaneal bone. The swelling due to oedema might obscure the findings of the palpation test. False negative diagnoses are often associated with postoperative haematoma, an avulsion fracture of the calcaneal bone or Achilles tendinopathy. The test has been more reliable for patients under anaesthesia than those awake (Maffulli et al. 1998). Furthermore, the palpation test has been used to evaluate chronic tendinopathy. Pain on palpation in the typical location has been found to be the best physical test for diagnosis of AT tendinopathy (Hutchison et al. 2013).

<table>
<thead>
<tr>
<th>Test</th>
<th>Sign of Achilles tendon rupture</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpation</td>
<td>Gap in the Achilles tendon</td>
<td>0.73 (0.65, 0.81)</td>
<td>0.89 (0.71, 0.97)</td>
</tr>
<tr>
<td>Single leg heel raise</td>
<td>Standing patient is unable to lift the heel against gravity</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Calf squeeze test</td>
<td>Only minimal plantarflexion of the ankle with squeeze of the calf</td>
<td>0.96 (0.93, 0.99)</td>
<td>0.93 (0.75, 0.99)</td>
</tr>
<tr>
<td>Knee flexion test</td>
<td>Foot falls into neutral or dorsiflexion when knee is flexed to 90°</td>
<td>0.88 (0.79, 0.94)</td>
<td>0.85 (0.66, 0.95)</td>
</tr>
<tr>
<td>Needle test</td>
<td>No movement in needle in calf muscles with passive ankle dorsiflexion</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Sphygmomanometer test</td>
<td>No pressure rise in sphygmomanometer with passive ankle dorsiflexion</td>
<td>0.78 (0.49, 0.94)</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

The single leg heel rise test was first developed in the 1940s. The patient is asked to stand on one leg and rise the body by lifting the heel off the ground. The knee should be straight. There might be some action due to the function of the posterior tibial, peroneal and the long toe extensors; however, this action is not sufficient for a single heel raise. A repetitive heel rise test has been used to estimate the neuromotor efficacy of the calf muscles by recording the active range of motion and number of heel raises. According to some reports, this test, instead of complete isokinetic
testing, is adequate for evaluation of the clinical outcome after AT tendon rupture. (Todorov et al. 2015)

The test based on squeezing of the calf muscles has been reported by Simmonds (Simmonds 1957) and later by Thompson (Thompson and Doherty 1962). The test is carried out with the patient in a prone position with both feet hanging freely from examination table. The examiner squeezes the gastrocnemius-soleus complex while observing the movement of the ankle. The test is positive if there is only minimal extension of the ankle. The calf should be squeezed at the level where the largest range of movement is achieved on the healthy side. The positive test has a significant association to total AT rupture with 96% sensitivity (Maffulli 1998).

The gastrocnemius muscle is connected to femoral condyles, and as a result, the tension of the AT is associated with the knee movement. This mechanism is utilized in the knee flexion test reported by Matles. Matles’ test is executed by asking a prone patient to flex both knees to 90°. If the AT is intact the foot will remain in a slightly plantarflexed position. (Matles 1975)

The integrity of the AT can be examined invasively with a needle test published by O’Brien. The test is performed by inserting a needle in the midline of the calf 10 cm proximal to the calcaneal insertion point. The needle should reach the AT. The test is positive if there is only minimal needle movement when the ankle is passively dorsiflexed. (O’Brien 1984)

Copeland reported another test for AT rupture, which is based on measuring the pressure of the calf muscles. A sphygmomanometer cuff is applied around the calf of the prone patient and inflated to 100 mmHg. The ankle is then passively dorsiflexed. If AT is intact the pressure will rise to approximately 140 mmHg. (Copeland 1990)

The accuracy of the palpation, calf squeeze, Matles, Copeland, and O’Brien tests have been compared in a study including 174 patients (Maffulli 1998). According to this study, all tests showed a high positive predictive value. At least two of the tests were positive in every AT rupture patient of the study. The most useful was calf squeeze test with 0.96 sensitivity, 0.93 specificity, and as a result, high positive likelihood ratio of 13.7. Consequently, a review article comparing different tests recommended the calf squeeze test as the most reliable to confirm diagnosis for AT rupture (Garras et al. 2012).

2.4.2 Imaging methods

Imaging methods should not be used routinely to diagnose acute AT ruptures. In uncertain cases, ultrasonography should be first performed (Dams et al. 2017). The plain radiographic examination is limited to evaluation of an avulsion fracture, Haglund’s deformity, or other bony pathology.

US is the primary imaging technique used to evaluate AT rupture because of the low cost and widespread availability of US equipment. During the examination, the patient is in the prone position with the ankle in dorsiﬂexion to induce tension of the tendon. However, possible hypervascular changes should be studied with the ankle
in flexion. The tendon should be examined in both longitudinal and axial planes (Gervasio et al. 2013). An acute AT rupture is defined by retraction of the tendon stumps. There might be a small amount of fluid around the tendon. A partial tear is characterized by intrinsic tendon abnormalities, thickening and irregular contours of the tendon. As a result of stretched tendon fibers or intact plantaris tendon total AT rupture might be erroneously diagnosed as partial damage. Postoperatively, the AT is always thicker than normal. Signals of hypervascularity appear one month after the rupture and will disappear after 6 months (Gervasio et al. 2013). If necessary, the tendon can be studied dynamically by moving the ankle from plantarflexed to dorsiflexed position. In total AT rupture the tendon ends will separate with paradoxical movement contrary to partial tendon tears. Furthermore, full juxtaposition of the tendon ends is not possible in delayed ruptures (Therman et al. 1992).

![Longitudinal views of dynamic US examination demonstrating acute AT rupture.](image)

**Fig.2.** Longitudinal views of dynamic US examination demonstrating acute AT rupture. Dashed line represents variable gap between tendon ends.

MRI is hardly ever indicated for the diagnostic evaluation of acute AT rupture. It is time consuming, expensive and can lead to treatment delays (Garras et al. 2012). However, the patients whose injury occurred more than 4 weeks before evaluation might benefit from MRI. Many of these patients may have confusing results in physical examination as a result of scar bridging. In addition, MRI might be useful in
patients with a history of prior tendinopathy or for preoperative planning of revision surgery (Padanilam 2009). AT rupture is best evaluated in sagittal T2-weighted MR images. The complete rupture will demonstrate a gap with fraying of the tendon ends and hyperintensity due to oedema. The T1-weighted images will provide anatomic details. Although MRI can visualize tendon structure in detail, these results were generally not related to the clinical picture (Dams et al. 2017).

![Fig. 3. An acute AT rupture in sagittal T1 MRI demonstrating a gap between tendon ends. The retracted proximal part is tensionless and thickened. Oedema is visualized better in T2-weighted images.](image)

**2.5 TREATMENT**

The first description of conservative treatment of AT rupture originated in 1736 by Jean Louis Petit. He used a custom-made brace with good results. The brace was later improved by Alexander Monro, who developed the first functional treatment with removable splints (Klenerman 2007). The first controlled study comparing operative and conservative treatment was published in 1929 (Qenu and Stoianovich 1929). Operative treatment became the mainstream therapy used in the industrialized world during the last decades of the 20th century. Most trials published before 2005 preferred operative treatment due to a lower risk for rerupture compared to conservative treatment (Cetti et al. 1993, Möller et al. 2001). Since then, new high-
quality studies have emphasized the risks associated with operative intervention, and as a result, nonoperative treatment has again increased in popularity (Mattila et al. 2015). Regardless of decades of active AT research, debate about the best treatment modality continues.

2.5.1 Non-operative treatment

The spectrum of complications in operative and nonoperative treatment are different. Obviously, there will be no postoperative infections without surgery. On the other hand, the risk of tendon elongation and rerupture might be higher, especially if patients are non-compliant (Glazebrook et al. 2019). The treatment choice is optional. Frequently, nonoperative treatment is recommended in high-risk patients with low physical demands, whereas operative intervention is preferred in professional athletes. According to clinical practice guidelines in the USA, operative AT rupture treatment should be avoided in patients with diabetes and in patients who are older than 65 years, sedentary, obese, smokers, neuropathic, or who have other specific concerns for wound healing (Kou 2010). On the other hand, organized haematoma and adhesions in delayed and chronic ruptures might render nonoperative treatment unsuccessful. Consequently, operative treatment is recommended for these patients (Maffulli and Ajis 2008). In addition, research considering nonoperative treatment is limited to acute ruptures only; thus, delayed or recurrent ruptures should preferably be treated with surgical intervention.

Modern nonoperative AT rupture treatment involves functional bracing and early mobilization with immediate weight bearing (Gross and Nunley 2016). Controlled motion exercises are frequently started 1 to 2 weeks after injury. Results with functional bracing are better than with historical rigid cast immobilization (McCormack and Bovard 2015). However, functional rehabilitation requires either good patient education or regular contact with physical therapists. Traditional immobilization with rigid cast has remained merely as an alternative with non-compliant patients. In this treatment, the ankle was first immobilized in the plantar flexed position for several weeks. Next the cast was changed to neutral position for 3 to 5 weeks and weight bearing was allowed. According to a retrospective study, 86% of the patients had excellent or good results with this method (Wallace et al. 2004).

In principle, ankle plantar flexion should bring retracted tendon ends together. During the healing process, the tendon responds to stress by becoming stronger and stiffer. Controlled mechanical loading during immobilization promotes healing by inducing tenocytes, activating protein kinases and various other biological responses (Killian et al. 2012). For this reason, movement is currently widely believed to be an important component of rehabilitation. Good functional outcome requires the AT to heal under adequate tension. Initial dorsiflexion and later change to a neutral position have resulted in better aligned tendons in animal tests (Hillin et al. 2019).

The choice between operative and nonoperative treatment of acute AT rupture is still controversial. According to several trials, nonoperative treatment with
functional bracing and early weight bearing have resulted in similar functional outcomes as operative treatment (Willits et al. 2010, Barfod et al. 2014). Although, better muscle strength with operative intervention has been reported as well (Lantto 2016). According to a recent meta-analysis, operative treatment reduces the risk for rerupture (Deng et al. 2017). However, rerupture rates as low as 2% have been reported with modern functional treatment policies (Aujla et al. 2019). Another meta-analysis concluded that differences between treatment results seem subtle and that conservative treatment should be considered in centres that use functional rehabilitation (Soroceanu 2012).

### 2.5.2 Open surgical treatment

Operative treatment has frequently been recommended for healthy young patients with high physiological demands. Professional athletes are usually treated operatively (Caldwell and Vosseller 2019). Acute AT ruptures can be treated by utilizing either traditional open surgery or minimally invasive approaches. The open procedure is preferred with neglected ruptures and reruptures (Maffulli and Ajis 2008). In the literature, open operative treatment is frequently associated with a lower rerupture rate compared to nonoperative management. A recent systematic meta-analysis including ten RCTs and 19 observational studies found a statistically significant reduction in the rerupture rate. On the other hand, the risk for other complications was higher with operative treatment (Ochen et al. 2019). However, as a result of low absolute complication rates in previous review, 62 operatively treated patients were needed to avoid one rerupture. Accordingly, 30 operatively treated AT ruptures resulted in one extra complication compared to nonoperative treatment.

Traditional open AT rupture surgery can be carried out under general, regional or local anaesthesia. The patient is prepared in the prone position for the operation. Frequently, posteromedial incision is preferred. The paratenon sheet is opened and the ruptured tendon exposed. Usually, there is a gap and fraying of tendon ends. Haematoma and necrotic tissue are removed, and tendon ends are approximated and sutured. The repair should be performed with “overtightened” tension to allow impending lengthening that will occur during rehabilitation. Skin and soft tissues should be handled with care and the paratenon closed if possible.

The tendon sutures should be able to resist excessive lengthening and rerupture until healing has completed (Eliasson et al. 2018). Multiple tendon suturing techniques, such as the triple bundle, Krakow locking loop, Bunnell and Kessler techniques, have been used. According to a meta-analysis of eleven studies, Bunnell and Krakow sutures were significantly stronger than Kessler sutures in the middle part of the tendon (Yammine and Asso 2017). Suture material has a great influence on strength. Number 1 or 2 non-absorbable polyester sutures are frequently used, even though a study (Benthien et al. 2006) has indicated that polyblend sutures might provide greater strength. The cadaver studies that compare suturing techniques have certain limitations because the tendon is sectioned transversely, and effects on both vascularity and wound exposure are excluded.
Fig. 4. An open repair of acute Achilles tendon rupture. Tendon ends are typically stranded.

In addition to only suturing the tendon end-to-end together, sometimes different reinforcing procedures with fascial flaps or tendons have been employed. Currently, they are not recommended in primary operations for acute AT ruptures. However, according to case series, these augmentation techniques might be useful options for repairing large defects in chronic AT ruptures (Mao et al. 2015) and excessive defects associated with insertional AT ruptures. In particular, V-Y advancement flap and flexor hallucis longus tendon transfer have been found to be reliable for tendon defects ranging from 2 to 8 cm (Bevilacqua 2012).

Fig. 5. Suture techniques for an open AT surgical reconstruction: A) Kessler, B) Bunnel, C) Krakow locking loop and D) Triple Bundle -technique.
Table 2. Common augmentation techniques for tendon defect reconstruction.

<table>
<thead>
<tr>
<th>Reconstruction technique</th>
<th>Tissue used as reinforcement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silverskiöld</td>
<td>One gastrocnemius fascial flap</td>
</tr>
<tr>
<td>Lindholm</td>
<td>Two gastrocnemius fascial flaps</td>
</tr>
<tr>
<td>Lynn</td>
<td>Plamaris longus tendon</td>
</tr>
<tr>
<td>V-Y plasty</td>
<td>Gastrocnemius fascia</td>
</tr>
<tr>
<td>FHL-transfer</td>
<td>Flexor hallucis tendon</td>
</tr>
</tbody>
</table>

Postoperatively, the ankle has been either immobilized with a cast or removable brace. Several postoperative protocols have been used with different timings of functional exercises and weight bearing (Brumann et al. 2014). Just as in conservative treatment, there is currently a trend to start exercises and weight bearing earlier than before. According to a recent meta-analysis, there is no significant difference in the postoperative rerupture rate or other major complications in early controlled motion exercises compared to traditional non-weight bearing cast immobilization (Ochen 2019). The reported time to return to work and sport activities are shorter with early mobilization (Brumann et al. 2014). In addition, functional rehabilitation is associated with high patient satisfaction, and there are considerable practical advantages with early mobilization and weight bearing (McCormack and Bovard 2015).

2.5.3 Minimally invasive operative treatment

Percutaneous, minimally invasive and partially open techniques for AT rupture repair were developed to minimize the risk for postoperative infection associated with open surgery and to improve functional outcomes compared to nonoperative treatment. The first described percutaneous technique used six stab incisions and a Bunnell suture (Ma and Griffith 1977). Later, techniques have been modified several times to improve suture strength and to avoid sural nerve injury (Webb and Bannister 1999, Carmont and Maffulli 2008). Currently, a variety of percutaneous, minimally invasive and partially open procedures are used. Traditionally, they have been recommended for acute ruptures only (Bevilacqua 2012, Mao et al. 2015). However, delayed repair up to 30 days after AT injury has been successfully treated using percutaneous repair (Maffulli et al. 2020).

Minimally invasive AT rupture surgery is possible with local anaesthesia only, although regional anaesthesia is used frequently. The patient is prepared for the operation in the same way as for open surgery. Detailed techniques differ, but in general, multiple sutures are passed diagonally through the tendon to opposing stab incisions one after another. Once sutures in both ends of the ruptured tendon are prepared, they are tied together under tension with the ankle in full plantar flexion.
Sometimes intraoperative US has been used to verify tendon reconstruction (Lacoste et al. 2014). When necessary, limited open repair by midline incision is possible to ensure good apposition of the tendon ends. The sural nerve crosses the lateral border of the AT at 9–10 cm from the calcaneal bone and continues distally near the tendon. During the operation, the sural nerve might be injured by a stab incision or be trapped in the suture knot. According to a report, the risk of perioperative nerve injury might be reduced with endoscopic techniques (Thermann et al. 2001). However, there is no further evidence of better outcomes with the use of arthroscopic equipment, and the learning curve is long. Special devices to facilitate tendon suturing have been developed, such as Tenolig® and Achillon® mini-open suture systems (Davies et al. 2017). According to the literature, device-assisted suture systems are safe for acute midsubstance AT rupture repair (Bartel et al. 2014).

Currently, identical postoperative treatment protocols are widely recommended for minimally invasive and open AT rupture surgery. Early mobilization with a removable orthosis, and controlled motion exercises and weight-bearing are as safe as traditional immobilization (Groetelars et al. 2014). A review article that included five RCTs and seven retrospective trials to compare open surgery with percutaneous repair reported almost similar functional outcomes in both groups. However, the percutaneous technique had a statistically significant increase in the risk for sural nerve injury and a decreased risk for deep postoperative infection (Yang et al. 2017). Learning curve to master new operative technique in foot and ankle surgery is evident even after 75 patients (Walton et al. 2012). Nowadays, when the great majority of AT ruptures in Finland are treated nonoperatively, a new treatment technique would be difficult to deploy. As a result of minimal differences in outcomes, minimally invasive operative treatment for AT rupture patients cannot be generally preferred.

### 2.5.4 Complications

The main complications reported after AT rupture treatment are tendon rerupture, deep infection and deep vein thrombosis of the leg. According to a multicentre study in the USA, approximately 1 in 9 patients undergoing operative repair of an acute AT rupture developed a postoperative complication (Stavenuiter et al. 2019). While major complications are rare, the implications for the patient could be devastating. A review article reported the mean incidence rates of rerupture, deep infection and DVT to be 5%, 1.5% and 2.67%, respectively (Wu 2019). Complications have been associated with multiple risk factors. A complication rate as high as 42% has been reported for patients who had one or more of the following risk factors: diabetes, smoking, or steroid use (Bruggeman et al. 2004). Minor complications include superficial infection, sural nerve disturbance and skin adhesions with abnormal cosmetic defects. In addition, excessive alteration of tendon length associated with inferior functional outcome might be considered a complication.
2.5.4.1. Rerupture

AT rerupture is mostly the result of incomplete or delayed tendon healing. Healing is promoted by adequate apposition of ruptured tendon ends and early mechanical load (Killian et al. 2012). However, early load might predispose tendons to excessive lengthening or rerupture. In addition to mechanical factors, the soft tissue envelope, various blood and tissue cells, inflammatory mediators and extracellular matrix molecules are involved in the complex healing process. Most reruptures occur in the first months after treatment. According to a study in Finland, the median time to rerupture was 23 days after nonoperative treatment (Reito et al. 2018).

![Image of rerupture](image.png)

Fig. 6. Delayed reconstruction of recurrent AT rupture with FHL-transfer technique. Retracted tendon end (**) has been revised and flexor halluxis longus tendon (*) prepared. The tendon will be attached (arrow) into bony channel of calcaneal bone.

Historically nonoperative treatment has been associated with a high risk for reruptures. A meta-analysis reported that 14 years ago, rerupture risk was 1.7 - 5.4% after initial surgical management and 12.7 - 20.8% after conservative management (Khan et al. 2005). According to a more recent systematic review, operative treatment is associated with lower rerupture risk compared to nonoperative treatment, 2.3% and 3.9%, respectively. However, there was no significant difference found in studies that used functional rehabilitation with early range of motion (Ochen 2019). Clearly, rerupture risk is decreasing due to an increasing trend in early motion exercises. Full weight bearing in combination with inadequate orthosis, inadequate apposition of the tendon ends, and long delay before repair have been associated to high rerupture rate (Maes et al. 2006). In addition, long tourniquet and operative times have been associated with increased rerupture risk (Jildeh et al. 2018). However, a long operation time might be a consequence of severe trauma or an inexperienced surgeon.
Operative treatment is preferred in chronic and recurrent AT ruptures. Open reconstruction is widely recommended, although a small series of percutaneous tendon reconstructions has been published (Maffulli and Ajis 2008, Becher et al. 2018, Maffulli et al. 2020). The debridement of adhesions and fibrous tissue between tendon ends may leave a considerable defect. Adequate tendon length is a prerequisite for good functional outcome, and direct end-to-end repair is suitable for small defects only. For example, the Myerson classification has been used to select appropriate operational methods (Myerson 1999). Medium-sized gaps can be treated with tendon-lengthening procedures. Recently, large defects have been reconstructed with tendon transfers, autografts, allografts, xenografts, and synthetic grafts (Chen and Hunt 2019).

Table 3. Myerson’s classification for the reconstruction of AT defect. Nowadays flexor hallucis longus tendon is most frequently used in tendon transfer operations.

<table>
<thead>
<tr>
<th>Tendon defect (cm)</th>
<th>Preferred reconstruction method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 2</td>
<td>End-to-end repair and posterior compartment fasciotomy</td>
</tr>
<tr>
<td>2 – 5</td>
<td>V-Y advancement flap +/- tendon transfer</td>
</tr>
<tr>
<td>More than 5</td>
<td>Tendon transfer alone or with VY-flap</td>
</tr>
</tbody>
</table>

2.5.4.2. Deep infection

Deep postoperative infections might have devastating results for patients. In addition to antibiotics, operative treatment is frequently required. As a result of the tenuous blood supply and thin soft tissue envelope, the distal leg region is prone to surgical site infections and delayed wound healing. History of smoking, long operating time and high blood loss have been associated with elevated risk for infection (Jildeh et al. 2018). In addition, pre-existing medical comorbidities such as diabetes and vascular disease are associated with high infection risk (Dombrowski et al. 2019). Particularly prone to infections are open procedures. A systematic review including 29 trials between 1981 and 2017 reported a 1.5% incidence of deep postoperative infection (Wu et al. 2019). Studies including patients operated on using the percutaneous technique only have fewer infections (Yang et al. 2017).

Excessive swelling increases the risk for wound complications and might prevent the operation in the first 3–4 days after injury. Optimal timing was examined in a study that divided patients into three groups: those operated on less than 24 hours, 24 - 48 hours and more than 48 hours after injury. According to the results, no significant differences in complication rate or clinical outcome were found (Park et al. 2017). According to surgical experience, tissues should be handled with care, and excessive tension in skin should be avoided. Peritenon fascia sheet should be closed whenever possible.
The postoperative use of antibiotics has not been studied in AT rupture patients. However, because routine use of postoperative antibiotics does not decrease the incidence of surgical site infection in ankle fractures (Lachman et al. 2018), prolonged antibiotic prophylaxis might not be required in closed AT rupture treatment either. There is no definitive treatment strategy for postoperative AT infection. Frequently, deep infections require intravenous antibiotics and operative debridement. Infections combined with large soft tissue defects are a challenge for plastic surgeons. Reconstruction might require free tissue transfer. In addition, composite radial flap or anterolateral thigh flap in combination with palmaris longus tendon or fascia lata transfer have been used in selected cases (Soons et al. 2015). However, good results have been reported with simple wound debridement and vacuum-assisted closure followed by skin graft (Mosser et al. 2015).

2.5.4.3. Deep vein thrombosis

DVT is a common complication after lower limb immobilization. However, only a minor proportion are symptomatic. DVT during the immobilization period is an independent predictor of poor outcome in patients with an acute AT rupture (Arverud et al. 2016). The reported rate of DVT after AT rupture has been highly variable, from 6.3% to 34%. Obviously, the incidence of symptomatic and asymptomatic DVT should be reported separately. Hormonal contraception, previous DVT, older age, and male sex have been identified as risk factors for symptomatic DVT in a large nationwide registry study in Denmark (Pedersen et al. 2019). Another study including 115 operatively treated AT ruptures reported a 23.5% DVT rate in routine US examinations. Most DVTs were asymptomatic, and one third were diagnosed before surgical intervention. As in a previous study, age greater than 40 years was considered a risk factor. Most DVTs in this study were limited to the distal part of the leg, and only one patient experience PE (Makhdom et al. 2013).

Early mobilization does not prevent a high incidence of asymptomatic DVTs after AT rupture treatment. RCTs comparing early mobilization to cast immobilization reported DVT rates of 37% and 29% at 6 weeks, respectively. However, low patient-reported loading, high BMI and older age was reported to be risk factors for DVT (Aufwerber et al. 2020). Periodic pneumatic compression devices have been used to prevent DVT. However, in AT rupture patients immobilized with a brace they are impractical. According to RCT examining pneumatic compression in AT rupture patients the intermittent use of the device did not have significant effect on the incidence of DVT at 6 weeks posoperatively (Domeij-Arverud et al. 2015).

According to the literature, routine use of thromboembolism prophylaxis after AT rupture is controversial (Patel et al. 2012). However, a high level of suspicion for the signs and symptoms of DVT is recommended. Extended bed rest should be avoided, especially in patients older than 40 years (Makhdom et al. 2013). Proximal DVT and PE in AT rupture patients should be treated with systemic anticoagulation according to the general guidelines. Recently, US surveillance has been recommended for
certain low-risk patients with distal DVT (Robert-Ebadi and Righini 2017). However, this surveillance is not an option for AT rupture patients with braces or casts.

2.6 EVALUATION METHODS

Scientific research comparing different AT rupture treatment options is difficult without universally accepted outcome measures. Functional results should not be estimated by the incidence of rare major complications only, even though they are associated with inferior outcomes and increased medical expenses. On the other hand, even minimal differences in functional outcome might be significant for patients involved actively in sports. In general, outcome measures can be divided into two major categories: objective and patient-reported outcomes. Frequently, both are used in combination in AT scoring systems (Spennacchio et al. 2016).

2.6.1 Functional outcome

Adult tendon healing is characterized by scar formation with diminished mechanical properties. The ruptured tendon undergoes inflammatory, reparative and remodelling phases. Furthermore, there is compensatory hypertrophy in the adjacent muscles, hallucis longus and deep flexors (Heikkinen et al. 2017). These changes will appear whether the patient is treated operatively or not (Kilian et al. 2012, Schepull et al. 2012). The main objective of the treatment is to restore the functional properties of the AT. Additionally, the leg should be cosmetically adequate and painless with minimal risk for complications. Successful treatment is associated with appropriate surgical management and is limited by the ability of degenerated tissue to heal.

Inferior functional results, including muscle weakness and gait abnormalities, have been associated particularly with excessive AT elongation. The greatest amount of tendon lengthening in operatively treated patients occurs between 2 and 6 weeks after surgery (Okoroha et al. 2020). Occasionally, tendon elongation has been estimated by ankle ROM. However, the reliability of this test is weak (Silbernagel et al. 2012). Although AT length has been estimated in research projects by US or been measured more accurately by roentgen stereophotogrammetric analysis using implanted tantalum beads, there is currently no validated outcome measure for tendon elongation (Spennacchio et al. 2016).

AT rupture permanently reduces calf muscle strength compared to the uninjured side, and deficits of 12% - 18% have been reported at 14-year follow-up (Heikkinen et al. 2017). Several studies have estimated objective strength by using dynamometry (Keating and Will 2011, Huttunen et al. 2014, Young et al. 2014, Lantto et al. 2016). Mostly isokinetic and sometimes isometric measurements of the ankle joint with a power ratio with respect to the uninjured side have been reported. The dynamometry results in general are reproducible. However, the equipment and position of the patient during the test is poorly standardized, and consequently, comparisons
between studies are difficult. In addition, test results are only moderately correlated to functional performance (Augustson and Thomeé 2000).

Calf muscle size, measured either by circumference or CT-derived cross-sectional area (Möller et al. 2002), has been suggested to estimate functional recovery. A statistically significant association between calf circumference and isokinetic measures with a 3-year follow-up time has been reported (Rosso et al. 2015). However, another study with a 3-year follow-up and isokinetic strength evaluation reported excellent or good strength in 75% of the patients, whereas calf muscle size was normal only in 30% (Leppilahti et al. 2000).

The most common measurement of calf muscle endurance is the inexpensive and readily available heel-rise test. During the test, the patient should stand on one leg with a straight knee. The number of repetitions and the height of the rise can be determined. A study investigating the heel-rise test at 12 weeks after AT injury found that 49% of the patients were unable to perform a single heel-rise, which was associated with poor patient-reported outcomes and physical activity levels (Olsson et al. 2014). The results of the heel-rise test, tendon length and isokinetic measurements are associated with each other (Möller et al. 2002). The heel rise test has been recommended as a primary measure of functional recovery after AT rupture.

### 2.6.2 Clinical scoring systems

According to a review, at least 21 different scoring systems have been used to report the outcome of AT ruptures. Several scoring systems are specific to AT rupture, while others, such as the widely used AOFAS, are specific to anatomic regions or are completely general, such as the SF-36. Most AT specific scores include strength evaluations in addition to subjective outcomes. (Kearney et al. 2012)

Table 4. Several outcome scoring systems specific for an AT rupture.

<table>
<thead>
<tr>
<th>Hannover Achilles Score</th>
<th>Thermann Score</th>
<th>Leppilahti score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rupp Ahilles Tendon Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achilles tendon Total Rupture Score (ATRS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandelbaum and Pavanini Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achilles Tendon Evaluation Score</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The best choice for reporting results after AT rupture treatment is uncertain. According to the literature, the results should preferably be assessed with AT rupture-specific measures in combination with generic patient-reported outcomes.
Ceiling effect might be present when the maximum scores are attained relatively easy. Vice versa, floor effect arises when the low scores don’t scale in accordance with the AT rupture patient outcome. Ceiling effect degrades validity of several health monitoring surveys, such as SF-36 (McHorney and Tarlow, 1995). Accordingly, the effect of AT rupture in generic AOFAS-score and SF-36 is very limited (Ceccarelli et al. 2014). In addition, the correlation of AT specific scores, ATRS and Hannover Score, with clinical outcome 3 years after the AT rupture is weak (Rosso et al. 2013).

The Leppilahti score is the first disease-specific protocol for evaluating the outcome after AT rupture (Leppilahti et al. 1998). This scoring system combines both subjective symptoms and objective measures categorized in seven sections. The best possible outcome is 100 points. The original Leppilahti score requires isokinetic muscle strength measurement, which is not always readily available. However, some articles have used a modified scale without instrumented measurement (Neumayer et al. 2010).

Table 5. Leppilahti AT rupture outcome scoring system.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>15</td>
</tr>
<tr>
<td>Mild, no limitations on recreational activities</td>
<td>10</td>
</tr>
<tr>
<td>Moderate, limitations on recreational, but not daily activities</td>
<td>5</td>
</tr>
<tr>
<td>Severe, limitations on recreational and daily activities</td>
<td>0</td>
</tr>
<tr>
<td><strong>Stiffness</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>15</td>
</tr>
<tr>
<td>Mild, occasional, no limitations on recreational activities</td>
<td>10</td>
</tr>
<tr>
<td>Moderate, limitations on recreational, but not daily activities</td>
<td>5</td>
</tr>
<tr>
<td>Severe, limitations on recreational and daily activities</td>
<td>0</td>
</tr>
<tr>
<td><strong>Calf muscle weakness (subjective)</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>15</td>
</tr>
<tr>
<td>Mild, no limitations on recreational activities</td>
<td>10</td>
</tr>
<tr>
<td>Moderate, limitations on recreational, but not daily activities</td>
<td>5</td>
</tr>
<tr>
<td>Severe, limitations on recreational and daily activities</td>
<td>0</td>
</tr>
<tr>
<td><strong>Footwear restrictions</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10</td>
</tr>
<tr>
<td>Mild, most shoes tolerated</td>
<td>5</td>
</tr>
<tr>
<td>Moderate unable to tolerate fashionable shoes, modified shoes tolerated</td>
<td>0</td>
</tr>
<tr>
<td><strong>Active range of motion (ROM) difference between ankles</strong></td>
<td></td>
</tr>
<tr>
<td>Normal (&lt;6)</td>
<td>15</td>
</tr>
<tr>
<td>Mild (6-10)</td>
<td>10</td>
</tr>
<tr>
<td>Moderate (11-15)</td>
<td>5</td>
</tr>
<tr>
<td>Severe (&gt;15)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Subjective result</strong></td>
<td></td>
</tr>
<tr>
<td>Very satisfied</td>
<td>15</td>
</tr>
<tr>
<td>Satisfied with minor reservations</td>
<td>10</td>
</tr>
<tr>
<td>Satisfied with major reservations</td>
<td>5</td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>0</td>
</tr>
<tr>
<td><strong>Isokinetic muscle strength (score)</strong></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>15</td>
</tr>
<tr>
<td>Good</td>
<td>10</td>
</tr>
<tr>
<td>Fair</td>
<td>5</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
</tr>
</tbody>
</table>
The frequently used ATRS was published in 2007 (Nilsson-Helander et al. 2007). The patient should fill in the verified questionnaires independently. The score consists of ten items, each estimated 0 to 10 on a Likert scale. In contrast to the Leppilahti score, an ATRS result of 100 points indicates the worst possible outcome. The reliability and validity of the ATRS have been verified, and there are multiple translations to other languages (Carmont et al. 2013). Some authors have advocated ATRS as an outcome evaluation method after AT rupture (Kearney et al. 2012).

Table 6. Achilles tendon Total Rupture Score (ATRS) questionnaire. The ATRS has been translated and validated in multiple languages including French, Italian, Portuguese, Polish, Dutch, Norwegian, Greek, Turkish and Chinese.

<table>
<thead>
<tr>
<th>All questions refer to your limitations/difficulties related to your injured Achilles tendon.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mark with an X the number which matches your level of limitation!</td>
</tr>
<tr>
<td>1. Are you limited due to decreased strength in the calf/Achilles tendon/foot? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>2. Are you limited due to fatigue in the calf/Achilles tendon/foot? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>3. Are you limited due to stiffness in the calf/Achilles tendon/foot? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>4. Are you limited due to pain in the calf/Achilles tendon/foot? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>5. Are you limited during activities of daily living? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>6. Are you limited when walking on uneven surfaces? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>7. Are you limited when walking quickly up the stairs or up a hill? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>8. Are you limited during activities that include running? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>9. Are you limited during activities that include jumping? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>10. Are you limited in performing hard physical labor? 0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

2.7 RANDOMIZED TRIALS

RTCs crown the pyramid of evidence and may change the prevalent clinical practise. At least 31 RCTs investigating AT ruptures were published between 2000 and 2019. At the beginning of the millennium, research focused mostly on comparing operative and nonoperative treatment, whereas more recent studies have examined different motion exercises or weight-bearing policies. Unfortunately, the results are difficult to compare due to inconsistent outcome reporting. Caution should be used when comparing outcomes between studies or pooling data from multiple RCTs concerning AT rupture treatment. In addition, regardless the similar label in multiple RCTs, the actual intervention could be very different (Zellers et al. 2019). Nevertheless, all these RCTs are briefly reviewed in this chapter.
Table 7. RCTs investigating AT ruptures from year 2000 to 2019.

<table>
<thead>
<tr>
<th>Subject of the trial</th>
<th>Number of RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative versus nonoperative treatment</td>
<td>7</td>
</tr>
<tr>
<td>Augmented versus nonaugmented repair technique</td>
<td>3</td>
</tr>
<tr>
<td>Minimally invasive versus open surgical technique</td>
<td>3</td>
</tr>
<tr>
<td>Open versus percutaneous versus conservative treatment</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative early versus late mobilization</td>
<td>9*</td>
</tr>
<tr>
<td>Nonoperative early versus delayed weight bearing</td>
<td>5*</td>
</tr>
<tr>
<td>Platelet-rich plasma, intermittent venous compression</td>
<td>3</td>
</tr>
</tbody>
</table>

*One article included two independent RCTs (Costa et al. 2006).

2.7.1 Operative versus nonoperative treatment

Operative and nonoperative AT rupture treatment has been compared in seven randomized trials in the current century. The first RCT (Möller et al. 2001) in Sweden reported equal functional results, although the rerupture rate was exceptionally high, 20.8%, in the nonoperative group. However, conservative treatment in this study was impractical and long, with an eight-week immobilization period. In contrast, RCT (Twaddle and Poon 2007) with similar postoperative instructions for motion exercises and weight-bearing in both groups reported no significant differences in complications. The ATRS score has been used as the main outcome measure in one RCT (Nilsson-Helander et al. 2010). According to this study, the improvements in the ATRS scores were equal in both operative and nonoperative groups at 6 and 12 months. Moreover, RCT (Willits et al. 2010) comparing operative and nonoperative treatment with similar accelerated rehabilitation protocols in both groups reported no clinically relevant differences in functional outcome or Leppilahti score. However, soft-tissue-related complications occurred more frequently in operatively treated patients.

One RCT (Keating et al. 2011), which compared muscle strength estimated by dynamometry results, reported no significant differences between operatively and nonoperatively treated patients at the one-year follow-up. In contrast, a more recent RCT (Lantto et al. 2016) found better calf muscle strength over the entire ROM of the ankle joint in the operatively treated group. The isokinetic dynamometry results were 10% to 18% better in the operatively treated group at 18 months. However, there were no differences in the Leppilahti scores between the groups. The same research group published a later RCT (Heikkinen et al. 2017) assessing calf muscle volume and AT length using MRI. The results were logically consistent with those previously
reported. The nonoperative treatment was significantly associated with soleus muscle atrophy and AT lengthening compared to operative treatment.

Table 8. RCTs comparing rerupture risk between operative and nonoperative treatment of AT rupture from year 2000 to 2019. Rerupture risk is lower in operative treatment. However, 2.6% of the patients treated operatively had a deep postoperative infection.

<table>
<thead>
<tr>
<th>Study</th>
<th>Nonoperative</th>
<th>Operative</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Møller et al. 2001</td>
<td>4</td>
<td>1</td>
<td>5.17 (0.54 - 48.3)</td>
</tr>
<tr>
<td>Twaddle and Poon 2007</td>
<td>11</td>
<td>1</td>
<td>15.19 (1.89 - 122.2)</td>
</tr>
<tr>
<td>Metz et al. 2008 *</td>
<td>6</td>
<td>3</td>
<td>1.86 (0.43 - 7.94)</td>
</tr>
<tr>
<td>Nilsson-Helander et al. 2010</td>
<td>6</td>
<td>2</td>
<td>3.36 (0.64 - 17.5)</td>
</tr>
<tr>
<td>Willits et al. 2010</td>
<td>3</td>
<td>2</td>
<td>1.52 (0.25 - 9.39)</td>
</tr>
<tr>
<td>Keating et al. 2011</td>
<td>4</td>
<td>2</td>
<td>2.00 (0.34 - 11.6)</td>
</tr>
<tr>
<td>Lantto et al. 2016</td>
<td>4</td>
<td>1</td>
<td>5.17 (0.54 - 49.3)</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>12</td>
<td>3.54 (1.81 - 6.92)</td>
</tr>
</tbody>
</table>

*Mini-invasive operative technique

Minimally invasive and nonoperative treatment was compared in one RCT (Metz et al. 2008). According to the study, there were no statistically significant differences in complication rates between the groups. However, the mean time to return to work was significantly shorter in the operative group than in the nonoperative group, 59 days and 108 days, respectively.

2.7.2 Augmented versus nonaugmented reconstruction

Tendon flaps to reinforce acute AT reconstruction have not been recommended for a decade. Nevertheless, three RCTs comparing augmented and nonaugmented AT repair techniques have been reported since 2000. According to a low-quality RCT in Turkey, early mobilization might not be safe after nonaugmented repair. However, this conclusion is based on a group of 24 patients only, and the results are statistically insignificant (Tezeren and Kuru 2006). A statistically more reliable RCT in Finland compared simple end-to-end suturing with fascial flap-augmented repair with a one-year follow-up time. No significant differences regarding reruptures, pain, stiffness, ROM or calf muscle strength were found. Moreover, the operative time and incision were longer in the augmented group, 25 minutes and 7 cm, respectively (Pajala et al. 2009). Another RCT in Finland reported 14-year follow-up results. No differences were found in isokinetic plantar flexion strength or outcome scores (Heikkinen et al. 2016). As a result, complex augmented repair technique can be considered in delayed or recurrent ruptures only.
2.7.3 Minimally invasive versus open operative treatment

Three RCTs have compared open versus minimally invasive operative techniques after the year 2000. The first trial that included 66 patients and a minimum follow-up time of six months reported a 21% infection rate in the open surgery group. However, this study used an exceptionally long 12-week immobilization time (Lim et al. 2001). The second RCT compared a minimally invasive technique using the Tenolig® device to open operative treatment. The study included 40 patients and reported no remarkable differences regarding clinical, US or isokinetic results at medium-term follow-up (Gigante et al. 2008). The third RCT compared outcomes with the Achillon® device to traditional open operative treatment. No significant differences were found. Notably, only a preliminary report of this trial has been published (Kołodziej et al. 2013). In addition, recent pilot RCT (Manent et al. 2019) including separate branch for minimally invasive operative treatment with similar early weight bearing-bring protocols reported no difference between the groups. However, the study included only 34 patients, and outcome measures were unstandardized. As a summary, scientific evidence supporting the use of minimally invasive operative technique is questionable.

2.7.4 Postoperative treatment protocols

Nine RCTs examined different mobilization protocols in operatively treated patients. RCT (Kangas et al. 2003) comparing 6 weeks postoperative cast immobilization to early mobilization with a removable brace found no differences regarding pain, stiffness, subjective calf muscle weakness, footwear restrictions, range of ankle motion, isokinetic calf muscle strength, or overall outcome. However, isokinetic muscle strength results were slightly superior in the early motion group. The long-term results were reported later (Lantto et al. 2015a). The clinical and isokinetic strength measurements were similar between the groups at the 11-year follow-up. Identically, no significant differences between the cast immobilization and functional bracing were found after minimally invasive AT repair (Groetelars et al. 2014). On the contrary, an article including two independent RCTs (Costa et al. 2006) reported better functional outcome in patients with immediate weight bearing.

Two RCTs compared functional outcome using roentgen stereophotogrammetric analysis with implanted tantalum beads. The first RCT (Schepull et al. 2013) reported a higher elastic modulus with increasing tension in the early mobilization group compared to the rigid immobilization group. The second RCT (Eliasson et al. 2018) found no significant differences between the groups in tendon lengthening or muscle strength. Neither RCT reported clinically significant differences between the groups in patient-reported outcome scores or heel-raise test.

Neglected AT ruptures have been examined in one RCT (Jielile et al. 2016). Outcome measured by Leppilah蒂 score, was better in the early mobilization group compared to postoperative cast immobilization group. In addition, postoperative cast immobilization resulted in cases of ankle joint ankylosis and osteoporosis.
Rerupture risk in RCTs comparing early and delayed postoperative mobilization. Exact follow-up time and mobilization protocol varies from trial to another. Rerupture risk is lower with early mobilization.

Table 9. Rerupture risk in RCTs comparing early and delayed postoperative mobilization. Exact follow-up time and mobilization protocol varies from trial to another. Rerupture risk is lower with early mobilization.

<table>
<thead>
<tr>
<th>Study</th>
<th>Early mobilization</th>
<th>Delayed mobilization</th>
<th>Odds Ratio, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kangas et al. 2003</td>
<td>1</td>
<td>2</td>
<td>0.48 (0.04 - 5.65)</td>
</tr>
<tr>
<td>Schepull et al. 2013</td>
<td>1</td>
<td>0</td>
<td>3.0 (0.11 - 78.81)</td>
</tr>
<tr>
<td>Grotolairs et al. 2014</td>
<td>1</td>
<td>1</td>
<td>0.87 (0.05 - 14.60)</td>
</tr>
<tr>
<td>Lantto et al. 2015a</td>
<td>2</td>
<td>2</td>
<td>0.94 (0.12 - 7.50)</td>
</tr>
<tr>
<td>Jielle et al. 2016</td>
<td>0</td>
<td>6</td>
<td>0.07 (0.00 - 1.38)</td>
</tr>
<tr>
<td>Valkering et al. 2017</td>
<td>0</td>
<td>1</td>
<td>0.35 (0.01 - 8.85)</td>
</tr>
<tr>
<td>Eliasson et al. 2018</td>
<td>1</td>
<td>0</td>
<td>1.55 (0.06 - 39.31)</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>12</td>
<td>0.42 (0.15 - 1.15)</td>
</tr>
</tbody>
</table>

RCT (Kauranen et al. 2002) has examined recovering of the motor performance functions after AT rupture repair. There were no statistically significant differences in reaction time, movement speed or foot tapping speed between the early and delayed mobilization groups at 12 and 24 weeks postoperatively. AT metabolism after the operative treatment was examined in one RCT (Valkering et al. 2017). There was no significant difference in the heel-rise test between the early mobilization group and the cast immobilization group. However, good functional outcome was significantly associated with high local concentrations of glutamate and protocollagen type I measured by microdialysis. In addition, one study examined periodic pneumatic compression for 150 AT rupture patients. The intermittent pneumatic compression device was applied for 6 hours per day for two weeks. At six weeks, the incidence of DVD was 52% in the treated group and 48% in the control group (Domeij-Arverud et al. 2015). Finally, local injection of platelet-rich plasma at the end of surgical operation did not improve outcome (Schepull et al. 2011).

2.7.5 Nonoperative treatment protocols

Different rehabilitation protocols in nonoperatively treated patients were compared in 5 RCTs. First RCT (Costa et al. 2006) including both operative and nonoperative branch compared early mobilization with full weight-bearing to non-weight-bearing. No significant differences between the nonoperative groups were reported. The next RCT (Young et al. 2014) examined patients with 8 weeks of cast immobilization and 2 years of follow-up time. The patients were randomized into either non-weight-bearing or early weight-bearing groups. There were no statistically significant
differences between the groups in time taken to return work, Leppilahti scores, patient satisfaction, pain, or return to sports. A concurrent RCT (Barfod et al. 2014) examined the effect of early weight-bearing and controlled early motion. There was no difference in ATRS, heel-rise test or rerupture rate. However, health-related quality of life was better in the weight-bearing group at 12 months. The same author published dynamometry results (Barfod et al. 2015) one year later. The stiffness of the plantar flexor muscle-tendon complex in the terminal portion of dorsiflexion was significantly increased in the non-weight-bearing group. Medium-term results after nonoperatively treated AT rupture have been examined in one RCT (Kastoft et al. 2019). The patients were randomized into either non-weight-bearing or early weight-bearing groups. Both groups were mobilized early. No differences were found at the 4.5-year follow-up time.

Table 10. Rerupture risk in RCTs comparing nonoperatively treated patients with early- and delayed weight-bearing. All patients were mobilized early. Early weight-bearing is safe.

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Total</th>
<th>Odds-ratio (95% CI)</th>
<th>Odds Ratio, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costa et al.2006</td>
<td>1</td>
<td>22</td>
<td>1.19 (0.07, 20.21)</td>
<td></td>
</tr>
<tr>
<td>Young et al. 2014</td>
<td>1</td>
<td>32</td>
<td>0.53 (0.05, 6.17)</td>
<td></td>
</tr>
<tr>
<td>Barfod et al. 2014</td>
<td>3</td>
<td>29</td>
<td>1.44 (0.22, 9.37)</td>
<td></td>
</tr>
<tr>
<td>Kastoft et al. 2019</td>
<td>1</td>
<td>29</td>
<td>0.45 (0.04, 5.23)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>112</td>
<td>0.87 (0.28, 2.68)</td>
<td></td>
</tr>
</tbody>
</table>

Finally, the controversial platelet-rich plasma injection therapy has also been investigated in nonoperatively treated AT rupture patients. According to multicenter RCT (Keene et al. 2019) including 230 patients, nonoperatively treated AT rupture patients had no benefit from local platelet-rich plasma injection.
3 AIMS OF THE STUDY

I. Explore the mechanism of Achilles tendon rupture, the results of the operative treatment and the typical complications in ordinary surgical units.

II. Compare the functional results of two operative methods, tendon end-to-end suturing only versus suturing reinforced with a tendon flap after AT rupture.

III. Examine the incidence, age, sex and regional distribution of Achilles tendon rupture patients over a long time period using national registry data.

IV. Investigate whether some drug treatments during the preceeding one year are associated with Achilles tendon rupture.
4 ACHILLES TENDON RUPTURES IN SOUTH-EAST FINLAND BETWEEN 1986-1996, WITH SPECIAL REFERENCE TO EPIDEMIOLOGY, COMPLICATIONS OF SURGERY AND HOSPITAL COSTS

4.1 ABSTRACT

Background and Aims: The incidence of achilles tendon (AT) ruptures is increasing. The aim of the present study was to evaluate annual incidence, aetiology, operative complications and direct hospital costs of AT ruptures.

Material and Methods: A retrospective study of 93 consecutive patients operated on for AT rupture from January 1986 to December 1996 at Kuusankoski District Hospital (area with 92,500 inhabitants) was performed. During the observation period no patient with an AT rupture was treated conservatively.

Results: 95 AT ruptures were treated including one rerupture (1%) and one patient with two ruptures. There were 7 (7%) patients with an open AT rupture. The total annual incidence in the hospital area was 8.6 (±4.3) and for closed AT ruptures 8.0 (±3.8). The total incidence was 9.3 (±4.6) /10^5 and for closed AT ruptures 8.6 (±4.1) /10^5 inhabitants per year. Most of the injuries were sport related, the most frequent sport being volleyball. Patients operated for closed AT rupture had major surgical complications in 4.5% of the cases and the total complication rate was 11%. The average direct hospital costs per patient was USD 1375.

Conclusions: The incidence of AT ruptures is increasing in South-East Finland. The rate of major surgical complication was low (4.5%) and comparable with earlier studies.

4.2 INTRODUCTION

According to literature only few studies about the incidence of achilles tendon (AT) ruptures have been conducted. Earlier population based investigations about AT ruptures have been done in Sweden (Wahlby 1978, Nillius et al. 1976, Möller et al. 1996), in Finland (Rantanen et al. 1993, Leppilahti et al. 1996) and in Denmark (Levi 1997). During the years 1979-1994, the incidence for AT rupture appeared to increase considerably in Northern Finland (Leppilahti et al. 1996). The increasing frequency of AT rupture is also reported in Sweden (Nillius et al. 1976, Möller et al. 1996). Only few studies concerning hospital costs for AT rupture have been carried out.

The objective of this study was a) to determine the annual incidence of AT ruptures in the Kuusankoski Hospital in Finland, b) to estimate the direct hospital
costs of medical treatment for AT-rupture patients in our area,
C) to analyse the aetiology of AT-ruptures and
D) to analyse briefly the onset and type of complications.

4.3 MATERIAL AND METHODS

The material consists of all patients operated in Kuusankoski District Hospital for closed or open ruptured achilles tendon during the period of 1.1.86 - 31.12.96. Kuusankoski District Hospital is responsible for all surgical operations dealing with AT ruptures in an area of 92 500 inhabitants. The amount of population in the area did not change significantly during the observation period. During the study years all patients with AT rupture were treated operatively. This was checked by interviewing all the senior surgeons who worked at the Kuusankoski District Hospital during these years and were responsible for these patients. None of the surgeons has ever treated a patient with an AT rupture conservatively. The AT rupture diagnosis was made clinically in all cases and no preoperative ultrasonic evaluations were done. Operations were executed by 14 physicians. Four senior surgeons did 67% of all the procedures while numerous juniors did only a few procedures each.

All cases were identified in surgical-diary and the patients’ records were checked. All data was retrieved from the medical records. Three ruptures discovered during the elective surgery were excluded from the study. The direct costs for in-patient care and surgery and for out-patient care were calculated according to an official price list of the hospital fees in 1999. Indirect costs were not included. Results were reported as means and standard deviations. Comparisons between two groups were made by using Student’s t-test and the change in AT rupture incidence was analysed using Fischer’s linear regression test. Differences were considered significant at the 0.05 level. The complication frequencies were calculated only for closed AT ruptures to make it easier to compare the results with earlier studies.

During the operation the patients were placed in a prone position and a tourniquet was used. AT and gastrocnemius aponeurosis were revealed by one about 15 cm incision. The rupture was reinforced by using flaps of gastrocnemius aponeurosis or plantaris tendon. The tendon strips were mainly sutured with absorbable Kessler apposition sutures, unabsorbable sutures were used in only five cases. Plain sutureation without augmentation was used when AT rupture was open or only partial or it was too proximal to turn down gastrocnemius flaps. Drain was used only in few cases and the tourniquet was always released after the closure of the skin.

Postoperatively the leg was immobilised with the ankle in about 20° plantarflexion with a short plaster cast. After a few weeks another short walking cast with the ankle in a neutral position was employed. Weight bearing was allowed gradually after three weeks. Postoperatively patients visited the outpatient department a few times. Active ankle exercises, full loading and strengthening
exercises were allowed after mobilisation. There was no standard rehabilitation program.

4.4 RESULTS

4.4.1 Incidence

During the 11 years observing period the total of 95 AT-rupture operations were executed. Two patients were operated twice, one for rerupture and the other for fresh tendon rupture on the other side, thus the material consists of 93 patients. 72 (77%) of them were men and 21 (23%) women. The average age was 44 years (SD 14, range 15 - 83) and the median age 42 years.

In our study the incidence of closed AT-rupture increased (0.05 > p > 0.01). The year 1990 was exceptional with 13 new cases (Fig. 1). AT-ruptures were most frequent in January, February and October: one third of the ruptures occurred during these months. We identified 48 AT-ruptures on the left side and 47 on the right side. The AT rupture risk for men was 3.4 times higher than for women. Left-right-side-ratio for women was 9/12 and for men 39/35. Differences in the affected side were insignificant (p > 0.8). AT rupture was considered as partial in 8 cases, but in all of these cases the rupture affected at last 50 % of the achilles tendon.

![Figure 1. The annual incidence on closed Achills tendon ruptures.](image)

Annual incidence for all AT-ruptures in the Kuusankoski Hospital area was 8.6 (SD 4.3) and for closed AT-ruptures 8.0 (SD 3.8). The total incidence was 9.3 (±4.6) /10⁵ and for closed AT rupture 8.6 (± 4.1) /10⁵ people per year. Open AT rupture was found in 7% (7/95) of the cases. Incidence for closed AT rupture was highest in the age-group of 40-44 years and 61% (54/88) of injuries took place between the ages of 35 and 54. A second peak occurred in the age-group of 65-69 years. The distribution of closed AT-ruptures according to the age is demonstrated in Figure 2.
4.4.2 Mechanism of injury

AT-ruptures were related to sport activities in 62% (59/95) of the cases and to ball games in 52% (49/95) of the cases (Table 1). The most dangerous sport was volleyball with 22 acute AT-ruptures, the second was soccer with 8 casualties and the third was badminton with 7 cases. These three activities resulted in 45% (33/74) of all male AT-ruptures. An AT-injury during sport-activity was as common among males, 62% (46/74), as among females, 62% (13/21). Badminton and soccer related injuries were especially common among young men, whose average age was only 35 years (SD 8.2, range 22 - 48). Correlation between young age and AT injury during sport activity was statistically significant (p < 0.001).

Direct AT-trauma, either sharp tendon incision or contusion-type of trauma, produced 12% (11/95) of injuries. Blunt trauma correlated with old age, the mean age was 50 years (SD 10, range 44 - 65) in this group. The reason for most sharp injuries was broken glass. Trauma included alcohol intake in 5 cases and violence by other people in 2 cases.

Indirect distension of AT induced 24 % (23/95) of all injuries. Typical mechanism for this type of injury was a sudden and powerful dorsiflexion in ankle. In our material slipping on stairs, jumping over a pit or pushing the car were typical outsets. Contrary to sport injuries these kinds of injuries correlated (0.0025 > p > 0.001) with older age. The average age for patients in this group was 54 years (SD 15, range 23 - 83). The onset of AT rupture remained unclear in two cases.
Table 1. Achilles tendon ruptures according the mechanism of injury.

<table>
<thead>
<tr>
<th>Mechanism of injury</th>
<th>men</th>
<th>woman</th>
<th>total</th>
<th>total%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sport related injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>volleyball</td>
<td>18</td>
<td>4</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>soccer</td>
<td>8</td>
<td>-</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>badminton</td>
<td>7</td>
<td>-</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>basketball</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>tennis</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Finnish baseball</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>squash</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>combat sports</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>running</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>gymnastics</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>floorball</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>dance</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>jumping sports</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>13</td>
<td>59</td>
<td>62%</td>
</tr>
<tr>
<td>Non-sport related direct trauma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sharp incision</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>blunt trauma</td>
<td>4</td>
<td>-</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>3</td>
<td>11</td>
<td>12%</td>
</tr>
<tr>
<td>Non-sport related undirect trauma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>walking/fall over</td>
<td>10</td>
<td>3</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>jump/leap</td>
<td>7</td>
<td>1</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>falling down</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>5</td>
<td>23</td>
<td>24%</td>
</tr>
<tr>
<td>Other or unknown injury</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>21</td>
<td>95</td>
<td>100%</td>
</tr>
</tbody>
</table>

### 4.4.3 Treatment

Delay before coming to the hospital for non-electively operated AT rupture was three days or more in 12 cases. The reason for the delay was an incorrect primary diagnosis in six of the cases. Four wrong diagnoses were made in local Health Centres, one in our hospital and one in another hospital. Four patients did not contact the physician.
at first place and in two cases the primary diagnosis made in the local Health Centre was right, but the patient was not sent to hospital in proper time. Wrong diagnoses included partial AT rupture in two cases, one distorsion of leg and one oedema of unknown origin. These patients were often primarily treated with anti-inflammatory analgesics, soft banding and even lymphotherapy.

Operation was executed on 72 AT rupture patients on the same day they arrived. 22 patients were operated on the second day after admission. Most of these patients had come to the clinic late in the evening, which explains the one-day delay. One patient was operated on the third day after admission due to his anticoagulative medication.

The AT was strengthened in operation by using two turn down gastrocnemius flaps in 33/95 (35%) and one central flap from the gastrocnemius aponeurosis in 45/95 (47%). Plantaris tendon was used to strengthen the plastia in eight cases. The type of augmented tendoplastia remained unclear in 6/95 (6%) cases. Simple suturation was adequate in 11/95 (12%) cases.

Patients stayed in hospital on average 2.4 days (SD 1.2, range 1 - 6). Hospitalization time decreased during our observation period. Patients operated during the years 1986-1990 were in hospital on average 3.1 days (SD 1.2) - during the years 1992-1996 they stayed in hospital only for 1.9 days (SD 1.0).

Postoperatively the first plaster cast with ankle in about 20° plantarflexion was worn for an average of 3.8 weeks (SD 0.5, range 3 - 5). After that another short walking cast with the ankle in a neutral position was employed making the total immobilisation time on average 7.7 weeks (SD 0.6, range 7 - 9). Each patient visited the outpatient department on average 2.4 times (SD 1.0, range 0-9).

4.4.4 Complications

No complications were found in patients with an open or partial AT rupture. The following complication frequencies were calculated for 88 patient with closed AT rupture. According to our records 11% (10/88) of patients had surgical complications. In five cases these patients were operated with two flaps from the gastrocnemius aponeurosis and in four cases with one flap. The final outcome among all the patients was satisfactory, but complications resulted in prolonged sick-leave, extra hospital visits and one reoperation.

Minor complications occurred in 6.8% (6/88) of patients operated for closed AT rupture. Superficial infections were identified in four patients. Three cases were treated with per-oral antibiotics and one infection healed spontaneously. All infections were noticed in 3 - 7 weeks after the operation. Exceptional postoperational tenderness and swelling at AT area were involved in two cases, both patients were operated with two gastrocnemius flaps. These complications resulted in extra hospital visits.

Major surgical complications emerged in 4.5% (4/88) of the patients with closed AT rupture. Ultrasonic examination 11 weeks after the operation revealed large haematoma at the AT region of one patient, and this was treated conservatively.
Plaster cast immobilisation caused one deep distal thrombosis of leg and one temporary paresis of the peroneal nerve. The most serious complication was one rerupture which emerged 10 weeks after operation. A new Lindholm plastia-type operation was required. The reoperation led to superficial infection and prolonged sick-leave, but the final outcome was satisfying.

4.4.5 Direct hospital costs

The costs of treatment days of patients with an AT-rupture amounted to FIM 530 550; the outpatient department fees were FIM 165 020 and the total hospital costs were FIM 695 570 (Table 2). The average direct costs per patient were FIM 7322 or USD 1375.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>FIM per unit</th>
<th>Total FIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in hospital (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per 2 first treatment days</td>
<td>190</td>
<td>2 685</td>
<td>510 150</td>
</tr>
<tr>
<td>Cost per 1 extra treatment day</td>
<td>34</td>
<td>600</td>
<td>20 400</td>
</tr>
<tr>
<td>Outpatient at hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient fee, doctor visit and change of the cast</td>
<td>95</td>
<td>940</td>
<td>89 300</td>
</tr>
<tr>
<td>Outpatient fee, doctor visit and removing of the cast</td>
<td>95</td>
<td>600</td>
<td>57 000</td>
</tr>
<tr>
<td>Outpatient fee, doctor visit</td>
<td>39</td>
<td>481</td>
<td>18 720</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>695 570</td>
</tr>
</tbody>
</table>

4.5 DISCUSSION

There are only few epidemiological studies about the incidence of AT ruptures (Wahlby 1978, Nillius et al. 1976, Möller et al. 1996, Rantanen et al. 1993, Leppilahti et al. 1996, Levi 1997, Barfred 1973). These show an increase in the incidence in Western countries during the past few decades. Nillius et al. reported (at 1976) an increased incidence in Malmö, Sweden, between 1950 and 1973 with a peak-specific incidence of $8.5/10^5$ per year in the age-groups of 40 to 50 years. Between 1987 and 1991 in the same region the highest annual incidence was in the age-groups of 30 to 39 years ($30.3/10^5$) (Möller et al. 1996). Between 1973 and 1975 in Umeå, Sweden, the incidence was $3.9/10^5$ inhabitants (Wahlby 1978). Rantanen et al. (at 1993) reported
the incidence to be 2/10^5 inhabitants in South-West Finland during the years 1980 - 1991. The average incidence of AT rupture in Northern Finland increased from 2 ruptures/10^5 inhabitants between 1979 and 1986, to 12 ruptures/10^5 inhabitants between 1987 and 1994 with a peak incidence of 18/10^5 in 1994 (Leppilahti et al. 1996). In Copenhagen, Denmark, the annual overall incidence of AT rupture during the period of 1978 - 1995 was 13.4/10^5 inhabitants (Levi 1997). In the present study the annual incidence increased from 1 rupture/10^5 inhabitants in 1986 to 12 ruptures/10^5 inhabitants in 1996, the change was statistically significant (0.05 > p > 0.01).

In Malmö, Sweden, the age distribution was bimodal with a maximum incidence of sports injuries in the fourth decade of life followed by a second, but a lower peak of other injuries in the eight decade (Möller et al. 1996). During the period of 1987 - 1991 the incidence in the fourth decade showed a threefold increase and in the eighth decade a more than fourfold increase as compared to the period of 1950-1973 (Nillius et al. 1976, Möller et al. 1996). Further, Leppilahti et al. (at 1996) from Northern Finland showed a similar bimodal age distribution as in the study of Möller et al. (Möller et al. 1996) and as in our study.

Most of the patients with a closed AT rupture are men, the ratio varying from 2:1 to 19:1 (Carden et al. 1987, Zollinger et al. 1983). In our study the ratio was 3.5 : 1. The majority of these ruptures are related to sports, especially to ball games (over 60 %) (Nillius et al. 1976, Cetti et al. 1993, Jojza et al. 1989, Inglis et Scuko 1981, Winter et al. 1995,22). The frequency of these ball games varies in different countries: in Denmark and Sweden the most dangerous game is badminton (Wahlby 1978, Nillius et al. 1976, Cetti et al. 1994, Nistor 1981), in Germany soccer (Winter et al. 1995), and in Northern Finland, as in this study, volleyball (Leppilahti et al. 1996). According to our study a closed AT rupture in sports is correlated with young age (p < 0.001). AT ruptures are mostly situated unilaterally and a slight left leg predominance has been reported (Jozsa et al. 1989, Hooker 1963, Hattrup et Johnson 1985). In this study there was no significant difference in the side ratio (p > 0.8).

The treatment of AT ruptures is still controversial. Surgical repair is advocated by many authors as the incidence of rerupture is low and the functional result can be better compared with that of conservative treatment by plaster cast immobilisation (Nistor 1981, Krüger-Franke et Scherzer 1993, Wills et al. 1986, Zwipp et al. 1989). In the review article from Leppilahti and Orava (Leppilahti et Orava 1998) the complication rate of 4 083 patients treated surgically for closed AT-rupture was 12 % and of 514 patients treated conservatively 18 %. The rerupture rates were 1.4 % vs. 13.4 %. The rate of major surgical complications (rerupture, deep vein thrombosis, temporary paresis of the peroneal nerve, large postoperative haematoma at the AT region) was 4.5 % in the present study, as opposed to 6.9 % in Leppilahti (at 1996) and 3.5 % in the review by Cetti et al. (at 1993). In our operatively treated material the total complication rate for closed AT-rupture was 11 % and there was only one rerupture (1 %). The present study did not show any difference in complications between the patient groups which were operated with one or two gastrocnemial flaps.
One of the main goals was to determine the incidence of AT ruptures in an defined area. Kuusankoski District Hospital is the only hospital for acute injuries in the region. The nearest private hospitals are at distance of 130 km. With an acute trauma like AT rupture people are likely to go to the nearest hospital. In our material there are two patients from outside of our area. We think it is safe to presume that equal amount of patients from our area have been treated in other hospitals.

There are certain limitations in our study as a consequence of the retrospectively collected data. It is possible that some minor complications are not mentioned in medical records. However, patients with a cast immobilization on average for 7.7 weeks (range 7 – 9) visited the outpatient department on average 2.4 times, and thus it can be assumed that all major complications have been observed. Cost analysis of direct costs consists of approximations of the true costs. The actual costs are difficult to evaluate, even in prospective studies, since the daily hospital fees, operation costs and especially outpatient care costs are only approximations to the true costs. Bearing these shortcomings in mind, the mean direct hospital treatment cost per patient was USD 1375. We are considering another study focusing the actual costs of AT ruptures in the future.

Operative treatment of AT rupture is more expensive than conservative treatment. In the review by Cetti et al. (at 1994) the mean hospitalization time for operatively treated patients was 6.4 days, while the time for conservatively treated patients was 0.2 day. Consequently, the length of sick leave for operatively treated patients was 10.5 weeks and for conservatively treated patients 8.2 weeks. In this study the length of sick leaves was not determined, because the patients were not examined after their sick leave. When comparing different treatment costs, the higher frequency of reruptures in patients treated conservatively must be considered. In the present study the mean hospitalization time between 1986 and 1990 was 3.1 days, between 1992 and 1996 1.9 days, and on average 2.4 days (range 1-6).

In conclusion we have shown that the annual incidence of AT ruptures increased between 1986 and 1996 reaching a stable level in the last three years. We have treated all patients with an AT rupture operatively and the rate of major operative complications was low (4.5 %) and comparable with earlier studies.
5 SIMPE END-TO-END SUTURE VERSUS AUGMENTED REPAIR IN ACUTE ACHILLES TENDON RUPTURES: A RETROSPECTIVE COMPARISON IN 98 PATIENTS

5.1 ABSTRACT

We retrospectively compared the results in 98 patients with an acute achilles tendon rupture treated with an augmented tendon repair (n 59) to patients with an end-to-end suture (n 39) after an average follow-up 44 (22-69) months. 7 patients were operated on more than two weeks after the rupture, all with augmention. The complication rates in the augmention group were 0.1 and in the end-to-end suture group 0.2. We found no differences in subjective outcome or rerupture rate between the groups. In the augmentation group, the rate of complications was higher in those operated on after 2 weeks than in those operated on before. A simple end-to-end suture seems sufficient.

5.2 INTRODUCTION

The surgical treatment of Achilles tendon rupture is still disputed. Tendon adaptation with sutures only (Soldatis et al. 1997) has sometimes been combined with various augmentation procedures (Soma and Mandelbaum 1995). A few authors have have also reported success with percutaneous treatment (Webb and Bannister 1999) or use of synthetic materials to strengthen the rupture (Fernàndez-Fairèn and Gimeno 1997). In many cases, the choice of method is based on the surgeon's intuition and tradition. We found no randomized studies comparing the simple tendon adaptation technique and tendon repair with augmentation. Therefore, we retrospectively analyzed the outcome in patients treated with an end-to-end suture or also with an augmented tendon repair.

5.3 PATIENT AND METHODS

Between 1995 and 1998, all patients operated on for Achilles tendon rupture in two Finnish hospitals were selected from the surgical diary and their records were checked. Those with an open rupture or a rerupture were excluded, as also were 2 patients who died during the follow-up. The operation was regarded as delayed if the time from injury to surgery exceeded 2 weeks. The method was classified as a simple end-to-end suture if no fascial or tendon reinforcement was used, whereas
tendoplasty, according to Lindholm (1959), Lynn (1966) and Silfverskiöld (1941), was considered as augmented.

Table 1. Postoperative complications in 98 Achilles tendon ruptures.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Augmented repair n 59</th>
<th>End-to-end suture n 39</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rerupture (op)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Deep infection (op)</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Superficial infection</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Partial rerupture</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Insertional tendinopathy (op)</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Stiffness in the ankle (op)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Paresis of n.peroneus</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Large hematoma</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>

op surgically-treated complication

An augmented repair was used in 59 patients and a single end-to-end suture in 39. Their average age was 45 (25-83) years. The patients treated with an augmented repair were 5 years older than the others (p = 0.059, chi-squared test). The times from injury to operation were similar in both groups, 1.5 (0-210) days. 7 operations were delayed and these operations were all done with a fascial augmentation, using Lindholm’s method (1959). In both groups, the ankle was postoperatively immobilized with a below-knee plaster cast with the ankle in plantar flexion. Weight-bearing was allowed after the cast was changed with the ankle in a neutral position 3 weeks later. The average immobilization time was 45 (23-59) days. The augmented repair group was usually immobilized for 1 week longer (p < 0.05, chi-squared test).

All patients received a questionnaire regarding the subjective outcome and they were invited to attend the hospital’s out-patient department for both reexamination and clinical tests. Of the 98 patients, who were included in the study, 83 answered the questionnaire and of these, 75 were reexamined 44 (22-69) months after the surgery. The subjective outcome was estimated with the scoring scale developed for ankle fractures (Olerud and Molander 1984). A total score of 100 is the best result that could be achieved. The range of motion in the ankle joint and the maximal
circumference of the calf were measured bilaterally. The scar, tendon and the ability to do heel raises were examined.

5.4 RESULTS

18 postoperative complication occurred (Table 1). End-to-end suture group had fewer postoperative complications (10%) than augmented repair group (24%) with RR = 2.3 (95% CI 0.8 - 6.5) and p = 0.09 using the chi-squared test. Patients with delayed (>2 weeks) augmented repair had a higher risk (4/7) for complications than those operated earlier (10/52) with RR 3.0 (95% CI 1.3-7.0) and p=0.03 using chi-squared test. Both deep infections were seen in the delayed repair group. The surgical outcome concerning local tenderness, skin adhesions, scar and tendon thickness was better in the end-to-end suture group than in the augmentation group (Table 2). We found no difference between the two methods as regards the subjective score, the ability to do heel raises or the maximal circumference of the calf (p>0.4, t-test).

Table 2. Findings at follow-up

<table>
<thead>
<tr>
<th>Local changes</th>
<th>Augmented repair n 42</th>
<th>End-to-end suture n 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor scar, tendon thickness normal</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Slightly thickened tendon</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>Deformated tendon or disturbing scar</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Skin adhesions</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Local tenderness</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

5.5 DISCUSSION

It has been stated that the increase in the amount of collagen obtained by augmentation can strengthen the Achilles tendon and thus permit earlier weight bearing after the rupture (Zell and Santoro 2000). The disadvantages of this technique are deformation of tendon and a longer incision. The frequent wound problems are not unexpected, because the commonly used longitudinal incision passes through poorly vascularized skin (Haertsch 1981).

We found no differences in the subjective outcome score between the two groups, although tendon deformations and problems with the scar were more frequent in the augmented repair group. We had an infection rate of 8%, higher than that reported by others (2 - 7%, Cetti et al. 1993, Leppilahti 1996, Jozsa and Kannus 1997, Nyyssönen and Lüthje 2000). Infections were commoner in older patients and in
those operated on after 2 weeks. The high risk of complications in patients over 65 years has been reported elsewhere (Nestorsson et al. 2000). Our few cases of reruptures indicate no real difference between the groups. Previous authors (Nistor 1981, Bradley and Tibone 1990, Lo et al. 1997, Leppilahti and Orava 1998, Nyyssönen and Lüthje 2000) have reported rerupture rates between 1 - 3% after surgery. The highest risk of rerupture (21 %) has been reported among patients treated without surgery (Möller et al. 2001). According to our study simple end-to-end suture is safe and reliable treatment with low risk for complications.
6 THE INCREASING INCIDENCE AND DIFFERENCE IN SEX DISTRIBUTION OF ACHILLES TENDON RUPTURE IN FINLAND IN 1987-1999

6.1 ABSTRACT

Background and aims: There have been reports about the increasing number of Achilles tendon ruptures. The most of the reports are based on records in a few hospitals only. We wanted to verify the increasing trend by investigating the epidemiology of Achilles tendon rupture in a very large population.

Material and Methods: The retrospective data was collected from 1987 to 1999 in Finnish National Hospital Discharge Register. The study includes 7 375 tendon rupture patients. We recorded their age, gender, home district and the date of admission in a hospital.

Results: The incidence of operatively treated Achilles tendon rupture was 11.2/10^5. The number of the patients was increasing particularly in the old age-groups. The change during the study period was statistically significant (p=0.015). The females with a tendon rupture were on average 2-3 years older than men (p<0.01). The urban areas around the capital city had a higher occurrence of tendon ruptures than the rural areas (p<0.05).

Conclusion: The number of Achilles tendon ruptures is increasing, but the reasons for this remain unknown. The geographical variations in rupture rate might indicate the role of the urban life-style as a risk factor. One reason for the differences between the man and the women might be the different level of the sport activities, especially ballgames.

6.2 INTRODUCTION

The incidence of Achilles tendon (AT) rupture is possibly increasing in the western world. This assumption is based on a few population based investigations done in Sweden (Möller et al., 1996), Denmark (Levi et al. 1997, Houshian et al. 1998) and Scotland (Maffulli et al., 1999). The epidemiology of AT rupture has earlier been studied in Northern Finland (Leppilahti,1996), in Southeastern Finland (Nyyssönen et al., 2000), and in Southwestern Finland (Rantanen et al. 1993). All these Finnish studies revealed an increasing trend, however the results based on records in few hospitals only.

The diagnosis of an AT rupture is usually quite simple and unambiguous. The operative treatment has long been recommended for physically active patients. All
operatively treated patients in Finland are registered in hospital wards and entered in the National Hospital Discharge Register (NHDR).

We carried out a study to determine the annual incidence of the surgically treated AT rupture patients, their age- and gender-related distribution and the geographical variation in Finland during the time-period from 1987 to 1999.

6.3 MATERIALS AND METHODS

The NHDR maintains annual data from all the Finnish hospitals. The NHDR database includes all the patients admitted to the hospital. The visits in the outpatient departments or the emergency departments are not registered. We acquired the permission to use this database and collected data in NHDR from 1987 to 1999. The unique personal identification number allowed us to focus our analysis on the first recorded admission. The diagnostic classification system used in Finland before 1987 (ICD-8) was too unspecific for our purposes, thus data about all AT rupture patients from 1987 to 1999 was recorded. At the time of the study more recent data not was available to us.

We registered the admission date, age, gender and the home district of all the patients. It is possible that a patient was admitted in the hospital for more than once because of the same AT rupture. To exclude these cases we accepted only the first admittance within one year after the AT rupture. In 1999 there were about 5.2 million inhabitants in Finland. Finally, we had the regional population data for both men and women for every year of the study period. Thus the given absolute numbers and incidences of an AT rupture were not cohort-based estimates but true final results. The statistical analysis was done by using MS Excel®- and SPSS®-programs.

6.4 RESULTS

There were 7,375 AT rupture patients during the 13 year study period. The mean age was 42 ± 12 years and 79% of the patients were male. The average annual incidence of the surgically treated AT rupture was 11.2 /10^5 inhabitants. We found an increasing trend in the AT rupture rate and in the average age of the patients (Table 1).

The reported incidence of the AT rupture in Finland was clearly increasing (p=0.016, Pearsons correlation test). In 1987 the incidence was only 8.3/105 persons whereas in 1999 it was 14.8/105. The incidence increased considerably in the older age but the increase was noticeable even in the age group of 30 – 40 years (Fig. 1). There was no increase in the amount of the AT ruptures in patients under 30 years of age. During the study period the average age of the patients increased by 4 years. The average monthly amount of tendon ruptures ranged from 38 in December to 56 in November. We found no statistically significant seasonal variation.
Table 1. Common characteristics of the Achilles tendon rupture patients

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients (n)</th>
<th>Mean age (years)</th>
<th>In hospital (days)</th>
<th>Incidence (1/100 000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>408</td>
<td>39,1</td>
<td>3,1</td>
<td>8,3</td>
</tr>
<tr>
<td>1988</td>
<td>388</td>
<td>40,6</td>
<td>3,3</td>
<td>7,8</td>
</tr>
<tr>
<td>1989</td>
<td>413</td>
<td>40,9</td>
<td>2,9</td>
<td>8,3</td>
</tr>
<tr>
<td>1990</td>
<td>497</td>
<td>40,4</td>
<td>2,7</td>
<td>9,9</td>
</tr>
<tr>
<td>1991</td>
<td>538</td>
<td>40,6</td>
<td>2,5</td>
<td>10,7</td>
</tr>
<tr>
<td>1992</td>
<td>590</td>
<td>42,0</td>
<td>2,4</td>
<td>11,7</td>
</tr>
<tr>
<td>1993</td>
<td>660</td>
<td>42,0</td>
<td>2,3</td>
<td>13,0</td>
</tr>
<tr>
<td>1994</td>
<td>642</td>
<td>42,0</td>
<td>2,2</td>
<td>12,6</td>
</tr>
<tr>
<td>1995</td>
<td>607</td>
<td>43,2</td>
<td>2,1</td>
<td>11,9</td>
</tr>
<tr>
<td>1996</td>
<td>597</td>
<td>42,4</td>
<td>2,0</td>
<td>11,6</td>
</tr>
<tr>
<td>1997</td>
<td>605</td>
<td>44,0</td>
<td>2,1</td>
<td>11,8</td>
</tr>
<tr>
<td>1998</td>
<td>667</td>
<td>43,7</td>
<td>1,9</td>
<td>12,9</td>
</tr>
<tr>
<td>1999</td>
<td>763</td>
<td>44,4</td>
<td>1,9</td>
<td>14,8</td>
</tr>
<tr>
<td>Total</td>
<td>7375</td>
<td>42,2</td>
<td>2,3</td>
<td>11,2</td>
</tr>
</tbody>
</table>

Only 1% of the AT rupture patients were under 20 years old. The risk for an AT rupture increases sharply after the age of 25 years. The incidence is particularly high between 30 – 45 years decreasing steadily afterwards. Only 2% of the reported cases were over 70 years old. The average age for a man to have an AT rupture was 41.7 and for a woman 44.0 years, the difference is statistically significant (p<0.01, χ²-test). Between the age of 25 - 35 years there were only 15% females, whereas in the age group 40 – 60 years 23% were females (Fig.2).
Fig. 1 The annual number of the Achilles tendon rupture patients according to the age-group

Fig. 2 The age distribution of the Achilles tendon ruptures in men and women
There were differences between the main 22 hospital districts in Finland; the reported annual incidence of the AT rupture varied from 7.6/105 to 13.8/105 persons (p<0.05, $\chi^2$-test). The incidence was highest around the urban areas of the capital city (Helsinki) in South Finland (Fig.3). The sparsely populated rural areas in North and East Finland had relatively fewer AT ruptures. The proportion of the female patients was particularly small in some eastern areas and noticeable higher in some areas in western Finland. Although, these regions are quite small which might result in a statistical error. The average age in different regions ranged from 41 to 45 years. There was no correlation between the regional incidence of the AT rupture and the average age of the local patients (p>0.6).

**Annual incidence / 100 000**

![Map showing the regional distribution of Achilles tendon ruptures in Finland](image)

Fig.3 The regional distribution of the Achilles tendon ruptures in Finland.
The average hospital stay was 2.3 ± 2.2 days. The treatment of an AT rupture required on average 3 days in hospital in the beginning and 2 days in the end of the study period. The patients stayed in hospital for less than 2 days in the capital area. In some areas a few of the patients were admitted in hospital for exceptionally long period, over a month.

6.5 DISCUSSION

The incidence of the AT rupture has been reported earlier in Scandinavia (Möller et al., 1996, Levi et al. 1997, Houshian et al. 1998), in Scotland (Maffulli 1999) and in Canada (Suchak et al. 2005). The epidemiologic data has indicated increasing frequency (Leppilahti, 1996, Nyyssönen et al. 2000, Rantanen et al. 1993). Our nationwide study confirms the increasing trend. The increased AT rupture rate was evident particularly in the old age. In our study the incidence increased 159% in patients older than 40 years during the 13 year period. The increasing AT rupture rate in age group 40 - 49 years has been reported in Scotland (Maffulli et al. 1999), the rest reports are from a few hospitals only and they have not specified any age-related incidence. The sub-group analysis according to the age is possible only with a very large number of patients. In our study the AT rupture rate was highest around urban capital area. According to our knowledge no geographical variation has been reported before and the life-style related risk factors for an AT rupture have not been studied.

In our study the age distribution of the AT rupture patients had a peak incidence at the age of 39 - 40 years. Previously there have been reports about a second peak in the older age (Möller et al. 1996, Nyyssönen et al. 2000), which we did not observe. Women had no such sudden increase in the AT rupture risk at 20-30 years of age as men. The higher average age in women has been reported earlier in Scotland and in Canada (Maffulli 1999, Suchak et al. 2005). Most of the AT ruptures in young adults are associated with the sport activities (Nyyssönen et al. 2000, Leppilahti et al. 1998, Maffulli et al. 2003). In Finland the most common sports associated with an AT rupture are football ja volleyball (Nyyssönen et al. 2000). The change in the age distribution and the difference between a man and a woman might be explained by different sport activities?

The average age of the AT rupture patients in our study was comparable to the previous reports ((Möller et al. 1996, Houshian et al. 1998, Leppilahti 1996, Maffulli et al. 2003). During the 13 years of study period the age distribution of the whole population has changed, which might partly explain the increasing average age of the patients. Even though the patients were on average 4 years older than in 1987, they stayed in a hospital for one day less in 1999.

All our data is based on the National Hospital Discharge Register. According to our knowledge our material is the largest uniform database about AT rupture patients ever reported. The accuracy of the Finnish NHDR has been assessed before. The NHDR covers 95 - 100% of all the patients admitted in a hospital (Salmela et al.
The diagnosis in NHDR has been found completely correct in 96 - 97% of all the patients (Salmela et al. 1987, Lüthje et al. 1995). In addition, the data about the age and sex of the patients is even more accurate (Lüthje et al. 1995). Our study includes only those AT rupture patients who entered the hospital ward. We suppose there were some conservatively treated patients who visited the out-patient clinics only and thus are not included in our data. However, most of the patients were in physically active age range and were treated operatively. The national textbook of traumatology (Järvinen, 1987) recommended the operative treatment as the only alternative for an acute AT rupture and the conservative treatment was very rare during the years 1987 and 1999 in Finland.

According to our study we are convinced that the incidence of an AT rupture in Finland is increasing and women having an AT rupture are on average older than men. One reason for this might be the different level of sport activities. Besides there were fewer AT ruptures in rural areas which might indicate the role of daily physical exercise in developing Achilles tendinopathy. The number of AT rupture patients is increasing and they are older than before. In the old age the functional expectations and activity level are often low and comorbidities are frequent. We do need more research about the treatment of the AT rupture in the old age and about the indications of the operative treatment in high risk patients.
7 DRUG TREATMENTS ASSOCIATED WITH ACHILLES TENDON RUPTURE. A CASE-CONTROL STUDY INVOLVING 1118 ACHILLES TENDON RUPTURES

7.1 ABSTRACT

The incidence of Achilles tendon (AT) rupture, especially non-sport related rupture, is increasing, while the reasons for this increase are largely unknown. The association between AT rupture and the use of various drug treatments was studied. We collected AT rupture patients from the Finnish Hospital Discharge Register. We also acquired information about all the doctor-prescribed drugs they had purchased within one year before the rupture. For comparison, we randomly selected age- and sex-matched controls from the Finnish Population Register. There were 1118 AT rupture patients. Several drug groups had a statistically significant association with the AT rupture. Our study confirmed an association between fluoroquinolone antibiotics and AT rupture (OR 2.20, p=0.005). A statistically significant association of renin-angiotensin II receptor antagonists with tendon rupture (OR 7.59, p=0.003) was a previously unreported finding. The increasing incidence of AT rupture, especially in middle-aged and elderly patients, might partially be a consequence of the increased use of certain drug treatments. Some associations are probably explained by the symptomatic treatment of the painful tendon before the rupture.

7.2 INTRODUCTION

The number of Achilles tendon (AT) ruptures has been increasing in last two decades (Sheth et al. 2017, Lantto et al. 2015b, Huttunen et al. 2014, Ganestam et al. 2016). A recent large epidemiological study demonstrated that the annual incidence of AT rupture has increased in Canada from 18.0 to 29.3 per 10⁵ in a 10 year period (Sheth et al. 2017). An increasing incidence has also been reported in Finland (Lantto et al. 2015) and Sweden (Huttunen et al. 2014). However, the proportion of operatively treated patients has recently declined (Ganestam et al. 2016).

Most AT ruptures are sports-related (Scott et al. 2014). A significant proportion of ruptures is associated with ball games (Kannus et Natri 1997). The variation in sport activities might be one reason for the increasing incidence (Leppilähti, 1996). In addition, the risk for AT rupture may be increased in some medical conditions. Patients with hyperparathyroidism, familial hypercholesterolaemia, rheumatoid disease and renal transplants have an increased prevalence of tendinopathy (Ames et al. 2008).
A number of reports have described tendinopathy associated with fluoroquinolone antibiotics (Budny et Lev 2015, Stephenson et al. 2013). Some other medical treatments, such as the long-term use of glucocorticoids and aromatase inhibitors, have also been associated with tendinopathy (Kirchgesner et al. 2014). An increased risk of AT rupture has been reported among patients using statin treatments (Teichtahl et al., 2016). However, the reports about statin-induced tendinopathy are conflicting (Marie et al. 2008, De Oliveira et al. 2013). The specific pathophysiological mechanisms behind drug-induced tendon injury are unknown.

The reasons for the increased incidence of AT rupture, especially non-sport related rupture, are unknown. We investigated the association between AT rupture and various medical drug treatments in 1118 operatively treated AT ruptures and 1118 randomly selected controls. The aim of our study was to find out associations between drug treatments and AT rupture.

7.3 MATERIAL AND METHODS

The National Hospital Discharge Register (NHDR) maintains data on all patients in Finland. Every patient admitted into a hospital is included. The completeness of the NHDR for operatively treated patients is good (Sund 2012, Keskimäki et Aro 1991). We have previously collected NHDR data on AT rupture patients during the years 1987-1999. The epidemiologic data for these 7375 patients has been published earlier (Nyyssönen et al. 2008). For the current drug-related study, only the patients admitted during the years 1998-1999 were included. In case of multiple admissions within a year, only the first admission was accounted for. A total of 1118 AT rupture patients were eventually included.

In Finland, a doctor’s prescription is required for the purchase of most of the drugs. These drugs are registered by the National Health Insurance Institution (NHII). Data from 1998 to 1999 were used for the present drug-related analysis. We acquired information from the NHII database about all drugs used by the AT rupture patients within the year before the rupture.

For comparison, we randomly selected age- and sex-matched controls from the Finnish population registry (Official Statistics of Finland). Corresponding medical data was collected from the NHII for the control group. A total of 1118 AT rupture patients and an equal number of reference cases with similar drug-related data were selected.

The drugs in the NHII database are referenced by their international Anatomical Therapeutic Chemical (ATC) codes. The first three digits of an ATC code indicate the main category of a drug product. We classified the numerous ATC codes into these main groups.

Case-control data were expressed as means and standard deviations or frequencies and percentages. The statistical analysis was done by cross-tabulating the number of AT rupture patients and reference cases for each main group. The
odds-ratios with 95% confidence interval was calculated for each 3-digit ATC code to measure association between the groups. Some clinically interesting drugs were analysed to a precision of 4 -5 digits of their ATC. Because of the large number of statistical tests, the false discovery rate (FDR)-adjusted p-value was used to compare the statistical significance of the association between the medical treatment and AT rupture. FDR-corrected p-values less than 0.05 were set to indicate statistically significant results.

7.4 RESULTS

The average age of the AT rupture case-control pairs was 44.1 years (SD 12.9), and 21% of the pairs were female. The annual incidence of AT rupture in 1998-1999 was 13.9 per 100 000 people. The AT rupture patients and the reference cases used medical products from 68 different ATC main categories. According to the FDR-adjusted analyses, there was a statistically significant association with AT rupture for 8 of the main drug groups (Table 1).

Table 1. Drug groups that had a statistically significant association with AT rupture according to the medical data for 1118 case-control pairs.

<table>
<thead>
<tr>
<th>Drug group</th>
<th>ATC code</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin-angiotensin system agents</td>
<td>C09</td>
<td>95</td>
<td>60</td>
<td>1.64</td>
<td>0.039</td>
</tr>
<tr>
<td>Sex hormones</td>
<td>G03</td>
<td>102</td>
<td>61</td>
<td>1.74</td>
<td>0.013</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
<td>H02</td>
<td>87</td>
<td>24</td>
<td>3.85</td>
<td>0.000</td>
</tr>
<tr>
<td>Systemic antibacterials</td>
<td>J01</td>
<td>407</td>
<td>317</td>
<td>1.45</td>
<td>0.001</td>
</tr>
<tr>
<td>Anti-inflammatory agents</td>
<td>M01</td>
<td>411</td>
<td>252</td>
<td>2.00</td>
<td>0.000</td>
</tr>
<tr>
<td>Topical pain relievers</td>
<td>M02</td>
<td>150</td>
<td>45</td>
<td>3.69</td>
<td>0.000</td>
</tr>
<tr>
<td>Analgesics</td>
<td>N02</td>
<td>48</td>
<td>23</td>
<td>2.14</td>
<td>0.037</td>
</tr>
<tr>
<td>Drugs for obstructive airway disease</td>
<td>R03</td>
<td>101</td>
<td>59</td>
<td>1.78</td>
<td>0.010</td>
</tr>
</tbody>
</table>

7.4.1 Anti-inflammatory and analgesics group

Many of the AT rupture patients (38%) used systemic anti-inflammatory medication before the rupture (OR 2.0, CI 1.66 - 2.41). Topical pain relievers were used by 13% of the AT rupture patients (OR 3.69, CI 2.62 - 5.21). The analgesics group included opioids, antimigraine preparations and antipyretics. Commonly used salicylic acid derivatives and paracetamol are examples of drugs in this category.
These drugs were used by 4% of AT rupture patients (OR 2.14, CI 1.29 - 3.54). In the subgroup analysis, the use of salicylic acid derivatives was not associated with rupture (p=0.385).

### 7.4.2 Antibiotics group

The use of antibiotics was common among both AT rupture patients (36%) and the reference (28%) cases (Table 1). The risk for tendon rupture in the antibiotics group compared to the control group was moderate (OR 1.45, CI 1.21 - 1.73). In the subgroup analysis, tetracycline and beta-lactam antibacterials had no association with AT rupture, whereas cephalosporins, sulfonamides and quinolones were associated with AT rupture. The association was the highest for the fluoroquinolone group (OR 2.20, CI 1.28 - 3.76). Specifically, the use of norfloxacin and ofloxacin was common among tendon rupture patients (Table 2).

Table 2. AT rupture risk associated with different fluoroquinolone antibiotics. The entire fluoroquinolone group was associated with a significant risk for rupture (OR 2.20, CI 1.28 - 3.76, p=0.005).

<table>
<thead>
<tr>
<th>Generic agent</th>
<th>ATC code</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>J01MA02</td>
<td>17</td>
<td>14</td>
<td>1.22</td>
<td>0.587</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>J01MA06</td>
<td>12</td>
<td>4</td>
<td>3.02</td>
<td>0.045</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>J01MA01</td>
<td>11</td>
<td>3</td>
<td>3.69</td>
<td>0.032</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>J01MA12</td>
<td>1</td>
<td>0</td>
<td>3.00</td>
<td>1.000</td>
</tr>
<tr>
<td>Fleroxacin</td>
<td>J01MA08</td>
<td>1</td>
<td>0</td>
<td>3.00</td>
<td>1.000</td>
</tr>
</tbody>
</table>

### 7.4.3 Systemic corticosteroids and drugs for obstructive airway disease

Both systemic corticosteroids and drugs for obstructive airway disease had a significant association with AT rupture. We analysed these two groups both in combination and independently because the simultaneous use of these products was common. The complete analysis revealed that only the use of systemic steroids was an independent risk factor for AT rupture (p <0.001).
7.4.4 Lipid modifying agents

No statistically significant association was found between lipid-modifying agents and AT rupture (OR 1.54, CI 0.96 - 2.48, p=0.465). Simvastatin, fluvastatin and lovastatin were the most-used drugs in both the AT rupture group and the control group.

7.4.5 Renin-angiotensin system-acting agents

The renin-angiotensin system (RAS) -acting agents group had a statistically significant (p=0.039) association with AT rupture. According to the subgroup analysis, the odds ratio was highest for the use of non-combined angiotensin II receptor antagonist products (OR 7.59, CI 1.73 - 33.36, p=0.003) (Table 3). At the time of the study, there were four renin-angiotensin II (RAS-2) receptor antagonist products on the market in Finland: losartan, valsartan, candesartan and eprosartan.

Table 3. AT rupture risk associated with renin-angiotensin system (RAS) -acting agents in the cohort of 1118 patients. The entire drug group was associated with a significant risk of AT rupture (OR 1.64, CI 1.17 - 2.29, p=0.039), which focused on renin-angiotensin II (RAS-2) receptor antagonist products.

<table>
<thead>
<tr>
<th>Drug group</th>
<th>ATC code</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain RAS receptor antagonist</td>
<td>C09AA</td>
<td>61</td>
<td>47</td>
<td>1.32</td>
<td>0.200</td>
</tr>
<tr>
<td>RAS receptor antagonist combinations</td>
<td>C09BA</td>
<td>20</td>
<td>16</td>
<td>1.25</td>
<td>0.614</td>
</tr>
<tr>
<td>RAS-2 receptor antagonist</td>
<td>C09CA</td>
<td>15</td>
<td>2</td>
<td>7.59</td>
<td>0.003</td>
</tr>
<tr>
<td>RAS-2 receptor antagonist + diuretics</td>
<td>C09DA</td>
<td>5</td>
<td>1</td>
<td>5.02</td>
<td>0.220</td>
</tr>
</tbody>
</table>

7.5 DISCUSSION

In our study, RAS agents were associated with AT rupture. This is a previously unreported finding. The risk was exceptionally high for RAS-2 receptor antagonists. Biochemically, RAS-2 receptor antagonists regulate serum aldosterone content, and no mechanism underlying a potential interaction with tendons is known. These drugs are used to treat hypertension and vascular disease. Notably, in our study, no other drug groups used in the treatment of hypertension were associated with AT rupture. During the study period, RAS-2 receptor antagonists were relatively new and infrequently used drugs in Finland, used by only 0.18% of the control group and 1.4% of the AT rupture group. In recent years, the situation has changed; RAS-2 receptor antagonists are currently much more common. According to the Finnish
NHII statistics (Finnish Medicines Agency Fimea, 2015) from 2015, these drugs are now used by approximately 6% of the Finnish population. The number of non-sport related AT ruptures in Finland has increased considerably over a 33-year period (Lantto et al. 2015). It is possible that the increase in non-sport related AT ruptures is related to the increased use of these drugs. A new study evaluating the relationship between RAS-2 receptor antagonists and AT ruptures is indicated.

The AT rupture patients in our study frequently used systemic anti-inflammatory medication (38%) and topical pain relievers (13%) prior to rupture. The statistically significant association between these products and AT rupture is presumably the result of tendon pain prior to rupture. Similarly, corticosteroid injections may have been used for Achilles tendinopathy. Corticosteroid injections reduce pain in short term, but the effect is temporary (Coombes et al., 2010). The injection treatment is associated with Achilles tendon atrophy which might cause tendon rupture (Hart, 2011). Due to our study design it is impossible to judge whether the rupture is a result of this treatment or just a coincidental event.

Our results confirm the association between the fluoroquinolones and AT rupture. The increased risk has been previously reported (Stephenson et al. 2013), and there are multiple case reports about fluoroquinolone antibiotics causing bilateral AT ruptures (Kawthaani et al. 2016). Fluoroquinolones have been available in Finland since 1987, and 6 drugs in this class were on the market during our study period. Ciproxin, norfloxacin and ofloxacin were the most commonly used generic molecules. In accordance with the results of a previous report (Kannus et Natri 1997), the risk of rupture was highest for ofloxacin in our study.

Our study has certain limitations. The data are very old, but the associations between the medical products and AT rupture are not time-related. The main results are still valid. The study of rare and sometimes unreported medical complications in a controlled manner requires a large patient cohort. Even among the 1118 case-control pairs, the number of patients using a single generic product is small; however, combining the drugs into larger groups might hide some individual associations. Economic reasons restricted the number of cases we could include; the gathering of the medical data was especially expensive. However, the statistically significant (p<0.05) association with AT rupture for the eight main drug groups indicates that the 1118 case-control pairs in our study is adequate (Table 1). Our data are representative for the Finnish population at the time of AT rupture for the study cohort because we used all of the patients in a nationwide register. Virtually all inpatient discharges from Finnish hospitals can be found from the NHDR whereas data concerning outpatient visits for conservative treatment might be unreliable (15). During the study period 99.4% of the records had right personal identification codes and a register validation study with hip fractures demonstrated 98% coverage and 98% sensitivity (Sund et al. 2007). The operative treatment decision is not based on the drugs the patient has used within a year before the AT rupture. Consequently, there is no reason to believe that the decision to operate has any effect on the statistically significant association between the drug treatment and the incidence of
the rupture. Our study does not include non-operatively treated AT ruptures. Those days the operative treatment was mainstream in Finland and conservative treatment became common not until 2007-2008 (Mattila et al. 2015). Furthermore, drugs that do not require a prescription are not included in our study. Most of these products are sold only in small quantities, and they are generally considered to be safe to use. Finally, cases of bilateral AT rupture occurring within one year are incorrectly accounted as a single case. However, bilateral AT rupture is rare.

7.6 PERSPECTIVE

The present registry study suggests that several drug treatments are associated with AT rupture. Some associations are probably explained by the symptomatic treatment of the painful tendon before the rupture. The increased risk for AT rupture in patients using ACE-2 antagonists is a new and interesting finding. The increasing AT rupture incidence, especially in middle aged and elderly patients, might partially be a consequence of increased use of certain drug treatments.
AT rupture frequently affects people in their active years. The topic has been the focus of intense research over the past decades, and treatment protocols have been continuously debated. In addition to RCTs, hundreds of clinical cohort series, case reports and biochemical research reports have been published.

8.1 INCIDENCE OF ACHILLES TENDON RUPTURE

According to numerous reports, the incidence of AT ruptures has been increasing in many countries. However, epidemiologic data are mostly limited to the industrialized world and acute ruptures only. The number of operatively treated AT ruptures in Finland has been available in the National Health Register since 1979. The increasing trend is also obvious in Finland. Long-term registry studies, such as ours, have certain limitations. The diagnosis of acute total AT rupture is usually obvious. It is highly unlikely that clinical diagnostics are currently better than before. As an assumption, operatively treated AT ruptures are more likely than conservatively treated patients to be included in the registry. The changing treatment policies, and thus the proportion of operatively treated patients, might produce incorrect results. However, during our epidemiologic study (III) period, the treatment method was probably very constant and changed to more conservative methods in the following years (Mattila et al. 2015, Sheth et al. 2017). Likewise, both the number of conservatively and operatively treated AT rupture patients in the Sweden have increased at the same time (Huttunen et al. 2014). In addition, current patients, especially older people, might be more active in sports and more likely than previous patients to contact health care providers. The significance of lifestyle related factors is very difficult to estimate. Furthermore, the demographics might change over time, and because AT rupture incidence is associated with age, the results should be corrected according to age distribution. Eventually, there seems to be convincing evidence that the incidence of AT ruptures has been increasing in our study period.

Most AT ruptures are associated with sports. In our study (I), 62% of the injuries were sport related. One reason for the increasing incidence of AT ruptures might be variations in sport activities. The number of older patients participating in physically demanding sport activities has increased. Our lifestyle has changed. According to Finnish military statistics, the physical fitness of young men has been decreasing, and body mass has increased over time (Santtila et al. 2006). Regular work-related physical exercise is currently uncommon. Excessive and occasional mechanical loading might predispose the AT to overuse injuries and tendinopathy. Lifestyle-related factors are difficult to measure objectively. However, in our study (III), the AT rupture rate was highest near the urban capital area, which might indicate an association with lifestyle-related factors.
8.2 TREATMENT OF ACHILLES TENDON RUPTURE

Currently, both operative and conservative treatment modalities are widely used. Mainly due to the high risk for soft-tissue complications, a shift towards non-operative treatment has been observed over the past ten years. Clearly, no postoperative infections can exist in conservatively treated patients. However, major complications are rare. The infection rate in operatively treated patients has been reported as low as 1.5% (Wu et al. 2019). Patients with high risk factors for infection, such as smoking, vascular disease and diabetes, have been frequently excluded from research projects. These patients, with presumably lower functional demands and older age, should be treated nonoperatively. In addition, large-scale randomized studies are limited to acute AT ruptures only; thus, the results do not address delayed ruptures or reruptures. The crucial question for acute AT rupture patients remains how to mitigate the elevated infection risk associated with operative treatment. Operative treatment and conservative treatment can be considered for certain acute AT rupture patients provided that appropriate rehabilitation protocols are deployed. The final decision between the treatment methods should be based on patient-specific factors and shared decision making.

Our original study (I) reported only a 1% rerupture rate with operative treatment. Operative treatment has been associated with lower rerupture risk compared to nonoperative treatment. A meta-analysis published 15 years ago reported 3 - 7 times more reruptures in nonoperatively treated patients (Khan et al. 2005). However, things might have changed. The benefit of early range of motion exercises in conservatively treated patients has now been recognized. According to a recent review, studies that used functional rehabilitation protocols had no significant differences in rerupture rate between operatively and nonoperatively treated patients (Ochen et al. 2019). Rerupture risk seems to be associated more with the rehabilitation policy than with the choice of treatment method. Furthermore, differences in functional outcomes using modern postoperative rehabilitation protocols are minimal (Deng et al. 2017). However, according to some results (Lantto et al. 2016, Heikkinen et al. 2017), operative treatment has resulted in better muscle strength and less muscle atrophy. Even minimal differences might be significant for professional athletes and people actively involved in sports.

Frequently, AT rupture treatment costs have been estimated with respect to hospital or society costs instead of patient’s point of view. Treatment that is economically feasible for one patient might not be effective for another. The patient’s costs are related to local healthcare arrangements, rendering international comparisons useless. From the hospital’s point of view, the direct treatment cost and possible major complications requiring new operative interventions are essential instead of functional outcome. The days of missed work are especially important from the standpoint of society or insurance companies. Our original study (I) included only direct hospital costs, $1.375 per patient. Considering the hospital costs,
operative treatment is probably more expensive than conservative treatment (Westin et al. 2018). Total costs for two years, including sick leave for nonoperative and operative treatment in the USA, have been reported as $13,936 and $13,412, respectively (Koltsov et al. 2020).

Our study (II) compared simple AT suturing to reconstruction reinforced with a gastrocnemius aponeurosis flap. There were no clinically significant differences between the groups. Currently, simple tendon suturing has displaced more complicated reconstruction procedures in the management of acute AT rupture. Different AT lengthening and tendon transfer procedures are nowadays preferred in reconstruction of large tendon defects only (Chen et al. 2019). Various minimally invasive or partially open procedures might be associated with a low risk for infections. On the other hand, the traditional open technique has a lower rate of sural nerve palsy, and disturbing palpable subcutaneous knots are rare. A recent meta-analysis found no significant differences for rerupture rates (Gatz et al. 2020). No definitive conclusion can be made regarding whether minimally invasive surgical treatment is better than open surgical procedures for acute AT rupture. On the other hand, traditional open surgical technique is more versatile. Open surgery is generally recommended for delayed ruptures that have a large gap or interposing scar tissue between the tendon ends. In addition to delayed ruptures, reruptures might require complex open reconstruction techniques. However, large-scale randomized trials have considered acute AT ruptures only. According to the literature, the optimal surgical technique for AT rerupture is controversial. In the absence of convincing evidence, the best surgical technique is probably the one in which the surgeon is most experienced.

According to the literature, early postoperative mobilization exercises and weight bearing seem to provide at least equal functional outcomes compared to cast immobilization (Kangas et al. 2003, Lantto et al 2015a). No significant differences in AT rerupture risk have been reported in recent studies (Ochen et al. 2019). Functional rehabilitation is associated with high patient satisfaction (McCormack and Bovard 2015). Walking is obviously easier without a heavy cast. However, certain limitations should be considered in deploying these practices. Frequently, the study protocols require many outpatient resources. In addition, the results are limited to compliant patients only. As a result, functional rehabilitation should be recommended for compliant patients whenever appropriate outpatient resources are available.

8.3 DRUG TREATMENTS ASSOCIATED WITH ACHILLES TENDON RUPTURE

A healthy AT endures repetitive loading without any structural damage. On the other hand, ruptured tendons have demonstrated pathologic lesions in microscopic examinations (Åström 1998). As a result, it seems evident that many AT ruptures are an obscure endpoint of progressive tendinopathy. During the previous decades, AT ruptures have increased. Consequently, AT tendinopathy should also have
increased. The reason for the deteriorating histopathologic changes before rupture is controversial. According to the literature, some medical drug treatments have been associated with tendinopathy. Thus, one reason for the increasing frequency of AT ruptures might be new drug products.

Despite thorough testing protocols, new drug products might have completely unexpected medical side effects. Sporadic events are difficult to verify. Frequently, a large number of patients or a long time period is required to investigate rare side events, such as AT rupture. In addition, statistical association with the drug and AT rupture does not always indicate a causal relation. AT rupture patients in our study (IV) frequently used systemic anti-inflammatory medication and topical pain relievers prior to rupture. This association presumably results from the treatment of tendon pain before rupture. Similarly, corticosteroid injections have a statistical association with AT rupture (Hart 2011). However, corticosteroid injections have been used to treat painful tendinopathy. Without prospective study, it is difficult to decide whether AT rupture is a true consequence of the treatment. Moreover, an association between AT rupture and drugs used to treat hypercholesterolemia, statins, has been suspected. However, tendon xanthoma patients have a high risk for a rupture, and xanthoma is common in familial hypercholesterolemia patients. Our study (IV) reported no association between the use of statin drug products and AT rupture.

According to the literature, AT rupture has been associated with fluoroquinolone antibiotics. However, the conclusion is mainly derived from observational studies and case presentations (Stephenson et al. 2013). Fluoroquinolone-induced tendinopathy was first reported in 1983. Occasionally painful bilateral tendinopathy occurs within hours of commencing fluoroquinolone treatment. Even low single doses of fluoroquinolone induce ultrastructural AT changes in animal models (Shakibaei and Stahlmann 2001). As a result of the rapid onset and low dose-effect relationship, direct toxic effects in collagen fibres have been suspected. Our study (IV) confirmed the association of fluoroquinolones and AT rupture. The risk of AT rupture was highest with ofloxacin treatment, in accordance with previous reports. The consumption of fluoroquinolones has increased during the same time period that the AT rupture frequency increased. However, the number of ruptures related to fluoroquinolones in Finland is far too low to significantly account for the total increased AT rupture rate. Nevertheless, more attention has recently been paid to fluoroquinolone-related adverse effects. After our study (IV), the European Medicines Agency recommended new restrictions on the use of fluoroquinolone antibiotics (European Medicines Agency 2019).

Our study (IV) reported a new and interesting association between RAS agents and AT rupture. The association was particularly significant in the RAS-2 group. These drugs are primarily recommended for the treatment of hypertension. For a century, the renin-angiotensin system has been known to be involved in the regulation of blood pressure and vasoconstriction, sodium intake and potassium excretion. Recently, new roles as pro-inflammatory and pro-fibrotic agents have been
reported. Angiotensin-II binding to its receptors mediates tissue damage by promoting mitochondrial dysfunction (Benigni et al. 2010). Angiotensin-II receptors are present in many tissues, including arterial and venous endothelial cells and internal organs. These receptors are entry points for SARS-CoV-19 virus in the lungs. It is not known whether angiotensin receptors are present in tendons. In our study (IV), AT rupture had no association with any other drug group used in treating hypertension. Thus, AT rupture seems to be associated, instead of high blood pressure, with RAS agents exclusively. During our study period, RAS-2 receptor antagonists were relatively new and infrequently used drugs. Currently, they are tenfold more commonly used in Finland, especially in middle-aged and elderly patients. As a result, AT ruptures should have increased correspondingly. The increasing frequency of non-sport-related AT ruptures since then has been reported (Lantto 2015b). According to our results, increasing AT rupture incidence might be partially explained by increased use of these drug treatments.

8.4 PERSPECTIVES FOR FUTURE RESEARCH

Until now, surgical research has been focused on comparing different treatment and rehabilitation protocols to each other. However, patients are not identical. The treatment method, which is excellent on average, might not be suitable for everyone. Instead of trying to determine which method is universally the best, perhaps we should concentrate more on various factors affecting the outcome and choice of an individual treatment protocol? A better understanding of postoperative complication rates and associated risk factors may enhance the decision-making processes in treating these injuries. Such an understanding requires large trials with different types of patients, including obese patients, smokers and variable age groups.

Economic awareness in the healthcare sector is increasing. An estimated 1,200 AT ruptures in Finland result in total costs of more than €10,000,000 annually. Regardless of physicians’ opinions, the results of surgical outcome alone will not be sufficient to convince political authorities and insurance companies. Funding decisions should be based on reliable data on the costs and benefits of the treatment. Our society needs more research focusing on the cost-effectiveness of the treatments that includes all aspects of care.

The RAS system, especially RAS-2 receptors, is involved in the inflammatory response and tissue healing sequence (Benigni et al. 2010). According to our results, there was a new statistically significant association of RAS agents with AT rupture. However, the number of patients using these drugs was quite low, and a new study about the relationship between RAS-2 receptor antagonists and AT ruptures is required to verify the association. The possible association of RAS-2 with tendinopathy raises the interesting fundamental question: What is the significance of the renin-angiotensin system to musculoskeletal degenerative changes altogether?
Healthcare information systems are developing rapidly. In the near future, massive amounts of structured data will facilitate automatic and continuous data harvesting and analysis. The results might be beyond human intelligence. This process also applies to orthopaedic research. Perhaps we will eventually be able to recommend a treatment programme tailored individually for every AT rupture patient according to the patients’ own risk factors and health-related objectives and, in contrast to the present, we will know for sure that the treatment option is the best.
9 CONCLUSIONS

I. A total of 62% of the AT ruptures were sport-related, and 52% occurred during ball games. The rate of major surgical complications, 4.5%, was low and comparable with literature.

II. Since AT reconstruction with gastrognemial aponeurosis flap compared to end-to-end suturing resulted in increased risk for local soft tissue complications a simple end-to-end suturing seems adequate.

III. The incidence of AT rupture has increased in Finland. On average, men were younger than women at the time of the injury. There were relatively more AT ruptures in urban areas.

IV. Many medical drug treatments are associated with AT rupture. We verified the high risk for AT rupture with fluoroquinolone antibiotics. The statistically significant association of RAS agents with AT rupture was a new and previously unreported finding. The increasing incidence of AT rupture might partially be a consequence of the increased use of certain drug treatments.
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Achilles tendon injuries have fascinated mankind since ancient Greece. This dissertation provides an overview to the surgical treatment of Achilles tendon rupture with special reference to epidemiology and predisposing factors associating Achilles tendon ruptures and medical drug treatments. According to our results increasing incidence of Achilles tendon ruptures might be partially explained by increased use of certain drug treatments.