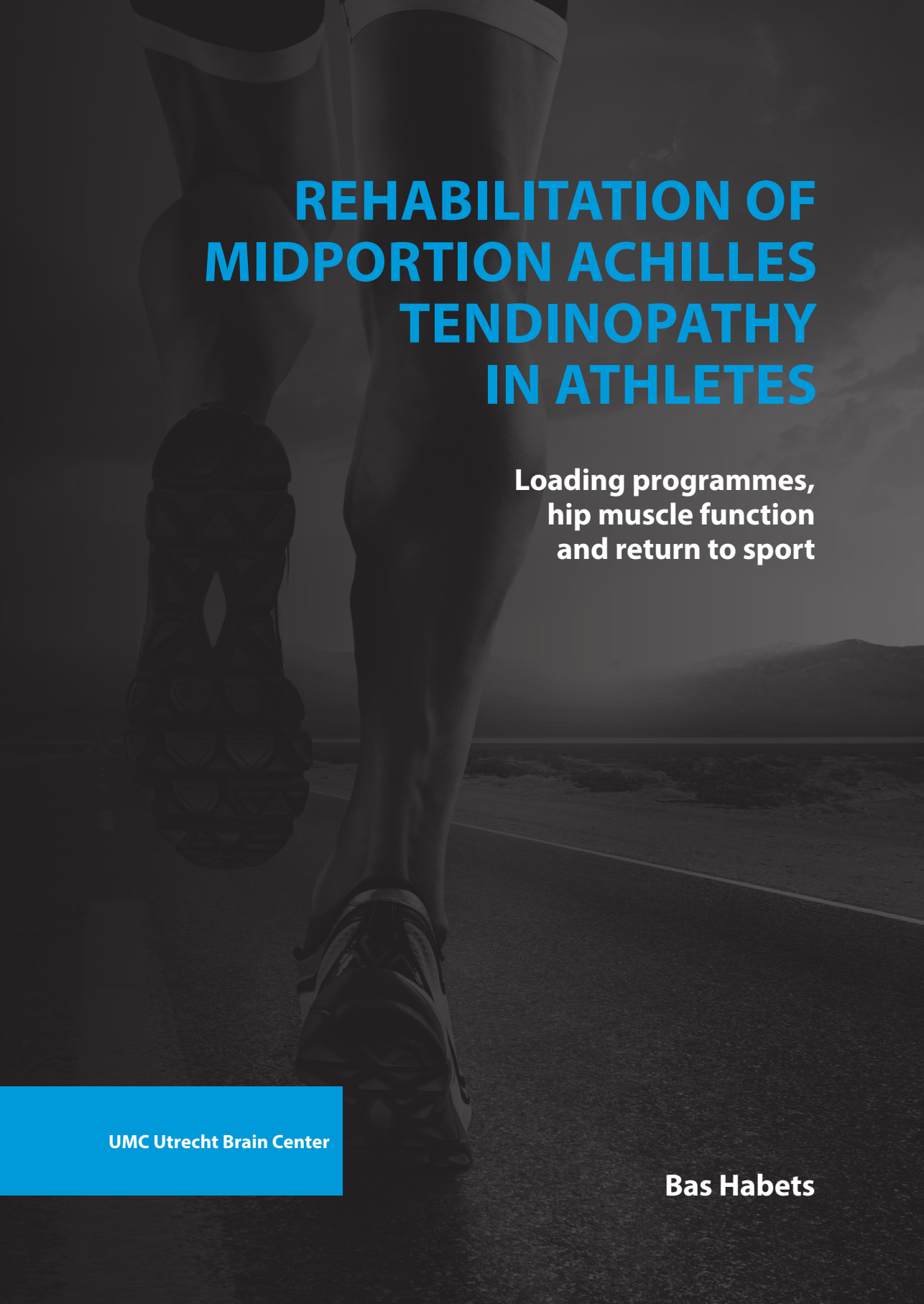

REHABILITATION OF MIDPORTION ACHILLES TENDINOPATHY IN ATHLETES

Loading programmes, hip muscle function and return to sport

UMC Utrecht Brain Center

Bas Habets

Rehabilitation of midportion Achilles tendinopathy in athletes

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Revalidatie van midportion achilles tendinopathie bij sporters

Oefenprogramma's, functie van de heupmusculatuur en sporthervatting

(met een samenvatting in het Nederlands)

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CONTENTS

CHAPTER 1

General introduction

Achilles tendinopathy (AT) is one of the most common overuse injuries of the lower extremity, mostly affecting athletes involved in running and jumping.[1] The term tendinopathy refers to a clinical syndrome, with a triad of pain, swelling and impaired (athletic) performance.[2] The scope of this thesis is midportion AT, in which symptoms are located 2-7 cm proximal to the calcaneal insertion, as opposed to insertional tendinopathy, where symptoms are located at the enthesis.[3] The midportion of the tendon is the most frequently injured site, accounting for approximately 80% of all cases,[4] and it is estimated that one third of these cases will develop bilateral symptoms.[5] Insertional tendinopathy is less common, affecting approximately 20% of the patients with AT.[4]

The introduction of this thesis will provide insight into basic anatomy and histopathology of midportion AT. Additionally, risk factors and epidemiological data of this injury are outlined. Finally, as a background for the specific aims of the thesis, an overview of different management options is provided, with a focus on conservative interventions.

ANATOMY AND HISTOLOGY OF THE ACHILLES TENDON

The Achilles tendon is the strongest tendon in the human body and plays an important role in absorbing the large forces that occur during locomotion and particularly sports.[6] It is the conjoint tendon of the separate muscles of the triceps surae muscle, distally inserting onto the calcaneus (Figure 1.1). In this way, it is involved in the motion of three joints, that is the knee, the talar and the sub-talar joints. Besides being the strongest tendon, the Achilles tendon is also one of the longest tendons.[7] It measures on average 15 cm, ranging from 11 to 26 cm. The thinnest part of the tendon is formed by the midportion, which is the part that is poorest vascularised.[8] The latter aspect could make it more prone to injury, yet this hypothesis has not been strongly scientifically supported.[9]

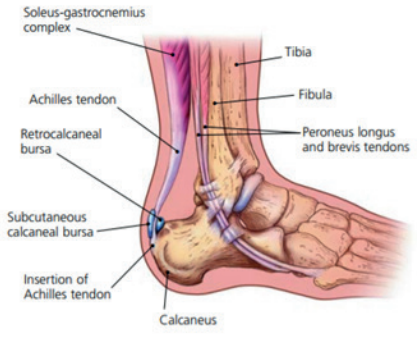

Figure 1.1 Lateral view of the Achilles region (reprinted with permission of R. L. Cannon)

The basic unit of the Achilles tendon is formed by collagen fibres that are surrounded by a fine sheath of connective tissue, called the endotenon (Figure 1.2). A group of collagen fibres forms a primary fibre bundle, and a group of primary fibre bundles in turn forms a secondary fibre bundle. Tertiary fibre bundles are composed of a bunch of secondary bundles and are considered to make up the tendon, surrounded by the epitenon.[10] The Achilles tendon has no synovial sheath but it is surrounded by the paratenon, a flexible connective tissue that allows for gliding.[11]

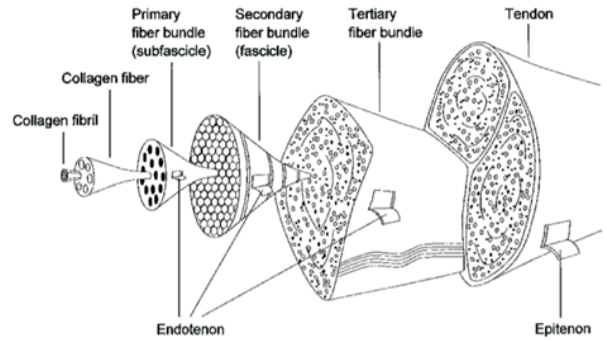

Figure 1.2 Structure of tendon tissue, from Kannus[10]

The fibres of the Achilles tendon are not strictly aligned. Instead, as they descend towards the calcaneal insertion, they display a twisted structure,[12,13] with a degree of torsion that may add up to more than 90 degrees.[14,15] There seems to be consensus that the direction of the twist is anti-clockwise in the right and clockwise in the left Achilles tendon.[14] Research has also shown that there is differential displacement between the different fibres arising from the medial and lateral gastrocnemius, and the soleus muscle.[16]

Like other tendons, the Achilles tendon primarily consists of 1) type I collagen fibres, predominantly longitudinally aligned and cross-linked to each other; 2) an extracellular matrix, consisting of proteoglycans, glycoproteins and glycosaminoglycans; and 3) cells, mostly formed by tenocytes that are involved in the synthesis of both collagen fibres and the matrix.[10,17] Additionally, elastin accounts for 1%-2% of the tendon, and small blood vessels run longitudinally through the tendon.

With its specific structure, the Achilles tendon is uniquely designed for storage and release of energy during locomotion and sport.[18] It can withstand extreme loads as high as 12 times the body weight.[19,20] However, the distinct structure may also predispose the tendon to (overload) injury.

Mechanical load will usually result in synthesis of collagen in the tendon, but research has indicated that collagen degradation occurs within the same time period.[21] In the first 24-36 hours after exercise, this results in a net loss of collagen, while a net synthesis of collagen occurs 36-72 hours after exercise (Figure 1.3).[17] A myriad of other structural responses appears to occur following different types of exercise, but it is currently unknown whether these changes are load dependent and either adaptive or maladaptive.[22]

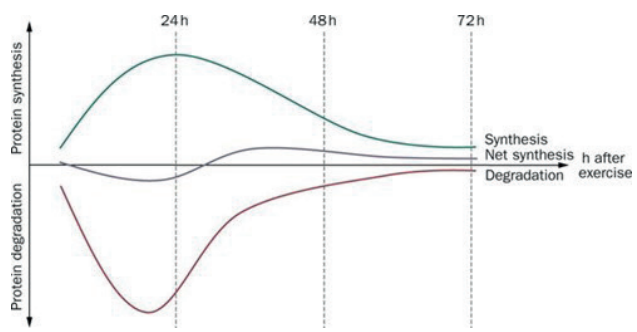

Figure 1.3 Schematic representation of collagen synthesis and degradation after a bout of exercise, from Magnusson et al.[17]

HISTOPATHOLOGY AND SYMPTOMATOLOGY

Historically, chronic tendon conditions had been recognised as an inflammatory condition, suggesting the presence of histopathological inflammatory features.[23] However, as researchers had failed to detect any classic signs of inflammation, in the late 1990s, Maffulli et al.[2] proposed to switch from tendonitis towards the term tendinopathy, referring to a clinical syndrome of pain, swelling and decreased performance. The term tendinosis was used only after histopathological confirmation of tissue changes.[3] In a consensus statement in 2019, a group of well-known worldwide clinical and research tendon experts from different disciplines agreed that the term 'tendinopathy' indeed should be used to describe persistent tendon pain and loss of function in relation to mechanical loading.[24] The use of the term tendinosis could not be recommended, as it is often unclear whether tissue changes are physiological (e.g. as a result of ageing) or pathological.

Several models exist to define tendinopathy.[23,25] Although these models describe tendinopathy in general, they also apply to midportion AT. These models roughly assume that tendinopathy is a failed healing response of the tendon to (chronic) overload. For

example, the Iceberg theory proposes that physiological adaptations, micro-ruptures and neurogenic inflammation may precede the actual symptomatic stage of tendinopathy.[23] A different model is the failed healing model proposed by Fu et al.[25] This model suggests that tendinopathy can be described as a three-stage process, including (initial) injury, failed healing and eventually clinical presentation.[25]

These explanatory models provide good comprehension of the pathophysiological process of AT, but the clinical usability appears to be limited, as they do not fully address the heterogeneity of clinical presentation. In 2009, Cook and Purdam[26] developed the continuum model, which was recently revised.[27] The continuum model describes three distinct stages of tendinopathy (Figure 1.4). It provides a framework for clinicians to direct their treatment.

The first stage is the reactive stage: acute tensile or compressive overload prompts a non-inflammatory cell response of the tendon, typically involving a proliferation and rounding of cells as well as increased production of large proteoglycans and glycosaminoglycans. As these proteoglycans bind water, a short-term homogeneous thickening of the tendon occurs, without loss of collagen integrity. The reactive stage is most often seen in young athletes and is accompanied by high pain levels and morning stiffness, with the tendon being swollen in a fusiform manner.

The second stage, tendon disrepair, describes a response similar to the reactive stage, yet with larger and more varied disruption of the matrix. There may also be neural ingrowth and hypervascularity. Although the disrepair stage can occur in the chronically overloaded tendon in young athletes, it may appear throughout a spectrum of ages. Pain and swelling as well as morning stiffness are also characteristic in the disrepair stage, combined with collagen disorganisation.

The end stage of the continuum model is the degenerative stage, in which large-scale breakdown of the tendon matrix occurs, areas of cell death become apparent, and ingrowth of neovessels and sensory nerves increases. The degenerative tendon is most common in the older population, but it may also occur in younger athletes who are exposed to chronic overload. The history often comprises repeated periods of tendon pain and stiffness that temporarily resolve when activity levels are decreased, but that flare up once the tendon load is increased. Although general thickening may be present, the degenerative tendon often shows focal nodular areas.

During the last decades, the concept of overload tendon injury has transformed from an inflammatory condition into a failed healing response of the tendon tissue; however, more recently there has been a trend towards reversal.[28] This is most likely due to advances in modern molecular techniques demonstrating the presence of several inflammatory mediators in tendinopathic tendons,[29-31] such as increased accumulation of macrophages and mast cells[29] as well as cytokines and prostaglandins.[32] Yet, it should be noted that the presence of these inflammatory mediators does not mean the presence of inflammation per

se. The role of inflammatory pathways in tendinopathy clearly needs to be further elucidated. Increased knowledge on these histopathological mechanisms can potentially direct novel models and resulting treatments.

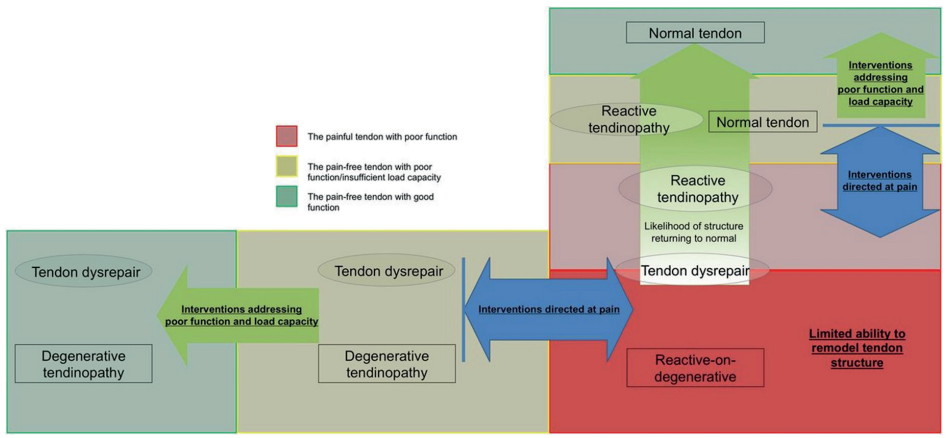

Figure 1.4 The revised continuum model for tendinopathy, from Cook et al.[27]

CLINICAL RELEVANCE OF THE CONTINUUM MODEL

The continuum model is based on accumulating intratendinous adaptations that are a result of acute or chronic overload.[26] However, pain can occur at any point in the continuum and is thus not merely linked to severe structural deformities. In the revised model, Cook et al.[27] suggested that clinically, two pain categories can be distinguished: 1) a first reactive presentation of symptoms following acute overload and 2) a reactive tendon on a (chronic) degenerative tendon pathology (Figure 1.4). Besides pain, both categories are associated with reduced load capacity of the tendon tissue. This means that pain should be considered and reduced in both categories, but interventions that target the load capacity of the tendon also appear to be crucial. In the early stage of the continuum, adequate load reduction and rehabilitation can 'push the tendon up the continuum' by normalising the tendon structure.[27] In the disrepair and mostly the degenerative stage, reversibility of the pathophysiological changes is limited. However, research has indicated that these changes only occur in certain areas of the tendon, and that these islands of degenerative tissue are still surrounded by sufficient healthy tendon tissue.[33] By reinforcing this healthy load-bearing tissue, the load capacity of the tendon can be restored to levels appropriate for both daily and sports activities. Consequently, rehabilitation of late-stage AT should focus on restoring load capacity instead of solely modifying symptoms.

INCIDENCE AND RISK FACTORS

Although AT does affect the sedentary, non-athletic population, the injury predominantly occurs in sports involving repetitive stretch-shortening cycle activities. An incidence rate of 9%-11% has been reported in various running disciplines,[34] with the highest incidence in long-distance runners according to recent numbers.[35] The cumulative lifetime incidence in former elite middle- and long-distance runners is estimated at around 52%.[36] With these numbers, AT accounts for one of the highest proportions of running-related injuries of the lower limb.[34,37]

De Jonge et al.[1] investigated the presence of AT in the Dutch general practitioner (GP) setting. They found an incidence rate of 1.9 per 1,000 patients, with no clear gender difference. The highest incidence was found for patients between 41 and 60 years of age (2.4 per 1,000 patients), suggesting that AT is more predominant in the adult population. This is in accordance with other studies.[38,39]

AT can be a long-lasting injury, and it is not unusual for patients to have intermittent symptoms for multiple years.[40] Recurrence rates tend to be high, with a re-injury rate of up to 27% in elite male soccer players.[41] Symptoms may be invalidating, and in approximately 5% of the cases, these long-lasting and disabling symptoms force athletes to end their career.[42]

A plethora of risk factors have been raised in the current literature. Sex,[43,44] age,[45] adipositas,[46-48] diabetes,[49] high cholesterol,[50,51] hypertension,[49] loss of tendon structure[52] and rheumatological diseases[53] are all considered to be associated with midportion AT. Additionally, biomechanical factors such as limited ankle dorsiflexion range of motion,[54-57] decreased plantar flexor strength,[54] altered gait kinematics[57-61] and altered proximal muscle activation[60,62] may contribute to development of the injury. Based on aetiological models, excessive loads (tensile, compressive or shear forces) are a considered key driver for the development of midportion AT,[63] with onset of symptoms often being caused by a spike in activity levels (e.g. weekly mileage or speed in runners). Indeed, training-related factors such as activity levels,[64-66] discipline,[44] training surfaces[66,67] and footwear[68] have been identified as potential risk factors.

A systematic review on biomedical risk factors for AT demonstrated that in an active population, high body mass index (BMI) and adverse lipid profiles may be important biomarkers.[46] Recently, Van der Vlist et al.[69] showed a set of 10 clinical risk factors for AT, of which moderate alcohol consumption, use of antibiotics (ofloxacin) and decreased plantar flexor strength were considered modifiable factors.

Unfortunately, many of the aforementioned risk factors were examined in case-control studies with high risk of bias, factors that clearly hamper a firm conclusion on causal relationships. Moreover, given the multifactorial nature of AT, it is likely that interaction between multiple factors occurs.[70]

DIAGNOSIS

Midportion AT is one of the simpler diagnoses to make; it is generally based on a thorough history and clinical examination. Pain at 2-7 cm proximal to the insertion is the cardinal symptom, with a close relationship to tendon loading.[38] Stiffness during the first steps in the morning is also characteristic and can be used as an indicator of tendon recovery.[38] Initially, pain may only be present after sports activity (grade 1), but with continued activity, this can evolve to pain at the beginning of sports activity that disappears with warming up (grade 2), and ultimately a continuous pain during rest and sports activity, interfering with someone's regular daily activities (grade 3).[71] Pain of midportion AT is predominantly localised; radiation to other regions seldomly occurs. Vague symptoms that encompass a larger region are suggestive of different or additional pathology.[38] The exact pain mechanism is still not fully understood, but scientific evidence suggests that both peripheral[72,73] and central pain mechanisms[73,74] play a role.

In addition to historical data, physical examination is used to verify the diagnosis of AT. Localised moderate or severe tenderness on palpation appears to be an accurate test,[75] although some authors argue that the clinical value is limited.[76] Palpation may also reveal a focal swelling at the level of the midportion. Other clinical tests such as the Royal London Hospital test and the painful arc sign can be used to verify the diagnosis.[77] To evaluate the clinical symptoms of AT, the Victorian Institute of Sports Assessment – Achilles (VISA-A) questionnaire is generally recommended.[78,79]

Load is one of the key drivers of tendinopathy. During clinical examination, a progressive loading stimulus is advised for symptom provocation as well as to investigate the load tolerance of the muscle-tendon complex. Repetitive heel raises are often sufficient to induce pain, but one can continue with double leg hops and single leg hops if symptoms cannot be sufficiently provoked.[80]

Imaging modalities can be helpful to identify the presence and extent of structural deformities in the tendon, but the link between structural abnormalities and symptoms seems weak.[39] Therefore, ultrasound and magnetic resonance imaging are not crucial for an accurate diagnosis, although they may be helpful in ruling out differential diagnoses such as peritendinitis, medial ankle tendinopathy or posterior ankle impingement.[81]

TREATMENT

Despite the expanding knowledge on pathophysiology and aetiology, optimal treatment of midportion AT remains difficult, particularly in competing athletes.[82] This is reflected by a plethora of different interventions, of which many are poorly supported.[83] Electrophysical modalities, such as extracorporeal shock wave therapy (ESWT)[84] and low-level laser therapy (LLLT),[85] may offer a safe and effective remedy to reduce pain, but their mechanism of action is not fully understood yet. Passive treatments, such as splinting/bracing[86,87] and specific massage techniques,[88] seem to have a limited effect. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroid injections can have a short-term analgesic effect,[89] but long term-effectiveness is often limited and evidence has shown adverse effects of corticosteroids.[90-92] Due to the developing knowledge on the pathophysiological process of tendinopathy,[23,25,26] new injection therapies such as sclerosing injections,[93] high volume-guided injections[94] and platelet-rich-plasma injections[95] have emerged. Many studies investigating these injection therapies have shown marked methodological shortcomings; therefore, the effectiveness of injection therapy is still controversial at best.[96,97] Thus, clinicians should be reluctant with routine use of these interventions as a stand-alone treatment for patients with AT.

EXERCISE-BASED INTERVENTIONS

It is generally agreed that exercise therapy for midportion AT should be the first line of management, for a minimum of 3-6 months.[80] In the early phase, appropriate load management should result in identifying and temporarily reducing provocative loading patterns (i.e. volume and type).[98] Complete rest is often contraindicated[99] and may be detrimental to load capacity of the muscle-tendon complex.[100] In addition to load management, there has been strong evidence for exercise-based interventions within the scientific literature, with a bias towards eccentric loading. This bias is mainly based on the research of Stanish and Curwin[101] and Alfredson et al.,[102] who showed that an isolated heavy-load eccentric loading programme for the plantar flexors yields significantly reduced pain levels and improved patient-reported function. Throughout the years, their findings have been repeatedly confirmed,[86,103-106] but the most effective training parameters for eccentric loading are still under debate.[107,108] Moreover, the results of eccentric loading appear to be less satisfying in certain subgroups (e.g. women[109] and non-athletic individuals[110]). This may explain why different exercise regimes have originated. For instance, Silbernagel et al.[99,111] proved a loading programme comprising both concentric and eccentric exercises to be effective, and more recently, Beyer et al.[112] demonstrated positive effects of heavy slow resistance training (HSRT) as a treatment strategy for AT. Thus, various loading programmes show improvement in clinical symptoms in individuals with AT, but there is no unequivocal evidence supporting that one loading programme is more effective than the other.[113]

Expansion of the evidence on the most effective loading programme will guide clinicians in choosing the most appropriate programme for their athletes.

Loading programmes are predominantly focused on strengthening the plantar muscle-tendon complex, whilst sports activities also require adequate functional performance of the proximal kinetic chain.[114] Decreased functional performance of the proximal kinetic chain can negatively influence lower extremity alignment, potentially causing a whipping action on the (medial aspect) of the Achilles tendon, thereby contributing to midportion AT. It can thus be hypothesised that omitting the proximal kinetic chain from exercise programmes for AT negatively affects the results of these interventions, but this hypothesis clearly needs further support. Scientific research unveiling a link between proximal kinetic chain dysfunction and AT can be a first indication that exercise-based interventions should also incorporate muscle groups of the proximal kinetic chain.

RETURN TO SPORT AFTER MIDPORTION AT

Despite the increasing evidence supporting exercise-based interventions in the treatment of midportion AT, successful resumption of sports activities during or at the end of the rehabilitation period can still be a challenge for both the athlete and the clinician. This is reflected by the relatively high recurrence rates found for this injury[41] and may be caused by the lack of well-delimited criteria to decide whether an athlete is completely recovered, both symptomatically and functionally. A clear description of criteria for the return-to-sports phase during rehabilitation would be helpful to aid clinicians in guiding athletes in this process.

AIMS AND OUTLINE OF THIS THESIS

With this thesis, we aimed to enlarge the knowledge base on conservative treatment of midportion AT in athletes, particularly focusing on the most effective loading programme, the potential role of the kinetic chain and criteria for return to sport. Our research will aid clinicians in choosing an appropriate intervention and evaluating when athletes are sufficiently rehabilitated to resume their previous sports activity levels.

First, we performed a systematic review to study the current evidence for the effectiveness of eccentric loading programmes to treat midportion AT **(Chapter 2)**. Second, we compared two commonly used loading programmes for chronic AT in a randomised controlled trial (RCT). We compared the traditional Alfredson isolated eccentric protocol, which is most frequently used in clinical practice, to the Silbernagel combined concentric-eccentric protocol, which has also been substantially supported within the literature. Research indicates that both programmes yield equivalent results, but to date this has not been verified in a comparative trial. **Chapter 3** describes the study protocol for this RCT. **Chapter 4** focuses on the effects of both loading programmes on clinical symptoms, and **Chapter 5** evaluates the effects on functional performance, such as plantar flexor strength and jump height. Because diminished strength of the relatively strong proximal hip muscle groups may hypothetically lead to increased Achilles tendon stress, and in this way may be linked to midportion AT, we conducted a cross-sectional study to investigate hip muscle strength in an athletic sample with AT **(Chapter 6)**. Finally, in **Chapter 7**, we provide a qualitative systematic review that explores the definition and the criteria for successful return to sport in the current AT research. In the general discussion **(Chapter 8)**, we interpret our research findings, including implications for clinical practice and recommendations for future research.

REFERENCES

1. De Jonge S, Van den Berg C, De Vos RJ, et al. Incidence of midportion Achilles tendinopathy in the general population. *Br J Sports Med* 2011;45(13):1026-8.
2. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. *Arthroscopy* 1998;14(8):840-3.
3. van Dijk CN, van Sterkenburg MN, Wiegerinck JI, et al. Terminology for Achilles tendon related disorders. *Knee Surg Sports Traumatol Arthrosc* 2011;19(5):835-41.
4. Sayana MK, Maffulli N. Insertional achilles tendinopathy. *Foot Ankle Clin* 2005;10(2):309-20.
5. Fahlström M, Lorentzon R, Alfredson H. Painful conditions in the Achilles tendon region in elite badminton players. *Am J Sports Med* 2002;30(1):51-4.
6. Muramatsu T, Muraoka T, Takeshita D, et al. Mechanical properties of tendon and aponeurosis of human gastrocnemius muscle in vivo. *J Appl Physiol* 2001;90(5):1671-8.
7. O'Brien M. The anatomy of the Achilles tendon. *Foot Ankle Clin* 2005;10(2):225-38.
8. Chen TM, Rozen WM, Pan WR, et al. The arterial anatomy of the Achilles tendon: anatomical study and clinical implications. *Clin Anat* 2009;22(3):377-85.
9. Astrom M, Westlin N. Blood flow in chronic Achilles tendinopathy. *Clin Orthop Relat Res* 1994(308):166-72.
10. Kannus P. Structure of the tendon connective tissue. *Scand J Med Sci Sports* 2000;10(6):312-20.
11. Pierre-Jerome C, Moncayo V, Terk MR. MRI of the Achilles tendon: a comprehensive review of the anatomy, biomechanics, and imaging of overuse tendinopathies. *Acta Radiol* 2010;51(4):438-54.
12. Szaro P, Witkowski G, Smigielski R, et al. Fascicles of the adult human Achilles tendon - an anatomical study. *Ann Anat* 2009;191(6):586-93.
13. Pekala PA, Henry BM, Ochala A, et al. The twisted structure of the Achilles tendon unraveled: a detailed quantitative and qualitative anatomical investigation. *Scand J Med Sci Sports* 2017;27(12):1705-15.
14. Edama M, Kubo M, Onishi H, et al. The twisted structure of the human Achilles tendon. *Scand J Med Sci Sports 2015;25(5):e497-503.*
15. Schepsis AA, Jones H, Haas AL. Achilles tendon disorders in athletes. *Am J Sports Med* 2002;30(2):287-305.
16. Finni T, Bernabei M, Baan GC, et al. Non-uniform displacement and strain between the soleus and gastrocnemius subtendons of rat Achilles tendon. *Scand J Med Sci Sports* 2018;28(3):1009-17.
17. Magnusson SP, Langberg H, Kjaer M. The pathogenesis of tendinopathy: balancing the response to loading. *Nat Rev Rheumatol* 2010;6(5):262-8.
18. Dean MN, Azizi E, Summers AP. Uniform strain in broad muscles: active and passive effects of the twisted tendon of the spotted ratfish Hydrolagus colliei. *J Exp Biol* 2007;210(Pt 19):3395-406.
19. Fukashiro S, Komi PV, Jarvinen M, et al. In vivo Achilles tendon loading during jumping in humans. *Eur J Appl Physiol Occup Physiol* 1995;71(5):453-8.
20. Komi PV, Fukashiro S, Jarvinen M. Biomechanical loading of Achilles tendon during normal locomotion. *Clin Sports Med* 1992;11(3):521-31.
21. Langberg H, Skovgaard D, Petersen LJ, et al. Type I collagen synthesis and degradation in peritendinous tissue after exercise determined by microdialysis in humans. *J Physiol* 1999;521(1):299-306.
22. Docking SI, Cook J. How do tendons adapt? Going beyond tissue responses to understand positive adaptation and pathology development: a narrative review. *J Musculoskelet Neuronal Interact* 2019;19(3):300-10.
23. Abate M, Silbernagel KG, Siljeholm C, et al. Pathogenesis of tendinopathies: inflammation or degeneration? *Arthr Res Ther* 2009;11(3):235.
24. Scott A, Squier K, Alfredson H, et al. ICON 2019: International scientific tendinopathy symposium consensus: clinical terminology. *Br J Sports Med* 2020;54:260-2.
25. Fu SC, Rolf C, Cheuk YC, et al. Deciphering the pathogenesis of tendinopathy: a three-stages process. *Sports Med Arthrosc Rehabil Ther Technol* 2010;2:30.
26. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. *Br J Sports Med* 2009;43(6):409-16.
27. Cook JL, Rio E, Purdam CR, et al. Revisiting the continuum model of tendon pathology: what is its merit in clinical practice and research? *Br J Sports Med* 2016;50(19):1187-91.
28. Kragsnaes MS, Fredberg U, Stribolt K, et al. Stereological quantification of immune-competent cells in baseline biopsy specimens from achilles tendons: results from patients with chronic tendinopathy followed for more than 4 years. *Am J Sports Med* 2014;42(10):2435-45.
29. Dakin SG, Newton J, Martinez FO, et al. Chronic inflammation is a feature of Achilles tendinopathy and rupture. *Br J Sports Med* 2018;52(6):359-67.
30. Millar NL, Hueber AJ, Reilly JH, et al. Inflammation is present in early human tendinopathy. *Am J Sports Med* 2010;38(10):2085-91.
31. Dean BJ, Gettings P, Dakin SG, et al. Are inflammatory cells increased in painful human tendinopathy? A systematic review. *Br J Sports Med* 2016;50(4):216-20.
32. Millar NL, Murrell GA, McInnes IB. Inflammatory mechanisms in tendinopathy - towards translation. *Nat Rev Rheumatol* 2017;13(2):110-22.
33. Docking S, Rosengarten S, Daffy J, et al. Treat the donut, not the hole: the pathological Achilles and patellar tendon has sufficient amounts normal tendon structure. *J Sci Med Sport* 2014;18:e2.
34. Lopes AD, Hespanhol Junior LC, Yeung SS, et al. What are the main running-related musculoskeletal injuries? A Systematic *Review. Sports Med* 2012;42(10):891-905.
35. Lagas IF, Fokkema T, Verhaar JAN, et al. Incidence of Achilles tendinopathy and associated risk factors in recreational runners: A large prospective cohort study. *J Sci Med Sport* 2020;23(5):448-52.

36. Kujala UM, Sarna S, Kaprio J. Cumulative incidence of achilles tendon rupture and tendinopathy in male former elite athletes. *Clin J Sport Med* 2005;15(3):133-5.

37. Francis P, Whatman C, Sheerin K, et al. The proportion of lower limb running injuries by gender, anatomical location and specific pathology: a systematic review. *J Sports Sci Med* 2019;18(1):21-31.

38. Cook JL, Khan KM, Purdam C. Achilles tendinopathy. *Man Ther* 2002;7(3):121-30.

39. Paavola M, Kannus P, Paakkala T, et al. Long-term prognosis of patients with achilles tendinopathy. An observational 8-year follow-up study. *Am J Sports Med* 2000;28(5):634-42.

40. van der Plas A, de Jonge S, de Vos RJ, et al. A 5-year follow-up study of Alfredson's heel-drop exercise programme in chronic midportion Achilles tendinopathy. *Br J Sports Med* 2012;46(3):214-18.

41. Gajhede-Knudsen M, Ekstrand J, Magnusson H, et al. Recurrence of Achilles tendon injuries in elite male football players is more common after early return to play: an 11-year follow-up of the UEFA Champions League injury study. *Br J Sports Med* 2013;47(12):763-8.

42. Kvist M. Achilles tendon injuries in athletes. *Sports Med* 1994;18(3):173-201.

43. Longo UG, Rittweger J, Garau G, et al. No influence of age, gender, weight, height, and impact profile in achilles tendinopathy in masters track and field athletes. *Am J Sports Med* 2009;37(7):1400-5.

44. Janssen I, van der Worp H, Hensing S, et al. Investigating Achilles and patellar tendinopathy prevalence in elite athletics. *Res Sports Med* 2018;26(1):1-12.

45. Maffulli N, Wong J, Almekinders LC. Types and epidemiology of tendinopathy. *Clin Sports Med* 2003;22(4):675-92.

46. Kozlovskaia M, Vlahovich N, Ashton KJ, et al. Biomedical risk factors of Achilles tendinopathy in physically active people: a systematic review. *Sports Med Open* 2017;3(1):20.

47. Gaida JE, Cook JL, Bass SL. Adiposity and tendinopathy. *Disabil Rehabil* 2008;30(20-22):1555-62.

48. Scott A, Zwerver J, Grewal N, et al. Lipids, adiposity and tendinopathy: is there a mechanistic link? Critical review. *Br J Sports Med* 2015;49(15):984-8.

49. Holmes GB, Lin J. Etiologic factors associated with symptomatic achilles tendinopathy. *Foot Ankle Int* 2006;27(11):952-9.

50. Tilley B, Gaida J, Cook J, et al. Is higher serum cholesterol associated with altered Achilles tendon structure or Achilles tendon pain in the general population? *J Sci Med Sport* 2015;19:e7-e8.

51. Abate M, Salini V. Mid-portion Achilles tendinopathy in runners with metabolic disorders. *Eur J Orthop Surg Traumatol* 2019;29(3):697-703.

52. McAuliffe S, McCreesh K, Culloty F, et al. Can ultrasound imaging predict the development of Achilles and patellar tendinopathy? A systematic review and meta-analysis. *Br J Sports Med* 2016;50(24):1516-23.

53. Jarvinen TA, Kannus P, Maffulli N, et al. Achilles tendon disorders: etiology and epidemiology. *Foot Ankle Clin* 2005;10(2):255-66.

54. Mahieu N, Witvrouw E, Stevens V, et al. Intrinsic risk factors for the development of achilles tendon overuse injury: a prospective study. *Am J Sports Med* 2006;34(2):226-35.

55. Rabin A, Kozol Z, Finestone AS. Limited ankle dorsiflexion increases the risk for mid-portion Achilles tendinopathy in infantry recruits: a prospective cohort study. *J Foot Ankle Res* 2014;7(1):48.

56. Kaufman KR, Brodine SK, Shaffer RA, et al. The effect of foot structure and range of motion on musculoskeletal overuse injuries. *Am J Sports Med* 1999;27(5):585-93.

57. Becker J, James S, Wayner R, et al. Biomechanical factors associated with Achilles tendinopathy and medial tibial stress syndrome in runners. *Am J Sports Med* 2017;45(11):2614-21.

58. Ryan M, Grau S, Krauss I, et al. Kinematic analysis of runners with Achilles mid-portion tendinopathy. *Foot Ankle Int* 2009;30(12):1190-5.

59. Donoghue OA, Harrison AJ, Laxton P, et al. Lower limb kinematics of subjects with chronic achilles tendon injury during running. *Res Sports Med* 2008;16(1):23-38.

60. Azevedo LB, Lambert MI, Vaughan CL, et al. Biomechanical variables associated with Achilles tendinopathy in runners. *Br J Sports Med* 2009;43(4):288-92.

61. Sancho I, Malliaras P, Barton C, et al. Biomechanical alterations in individuals with Achilles tendinopathy during running and hopping: a systematic review with meta-analysis. *Gait Posture* 2019;73:189-201.

62. Franettovich Smith MM, Honeywill C, Wyndow N, et al. Neuromotor control of gluteal muscles in runners with achilles tendinopathy. *Med Sci Sports Exerc* 2014;46(3):594-9.

63. Abat F, Alfredson H, Cucchiarini M, et al. Current trends in tendinopathy: consensus of the ESSKA basic science committee. Part I: biology, biomechanics, anatomy and an exercise-based approach. *J Exp Orthop* 2017;4(1):18.

64. McCrory JL, Martin DF, Lowery RB, et al. Etiologic factors associated with Achilles tendinitis in runners. *Med Sci Sports Exerc* 1999;31(10):1374-81.

65. Haglund-Akerlind Y, Eriksson E. Range of motion, muscle torque and training habits in runners with and without Achilles tendon problems. *Knee Surg Sports Traumatol Arthrosc* 1993;1(3-4):195-9.

66. Knobloch K, Yoon U, Vogt PM. Acute and overuse injuries correlated to hours of training in master running athletes. *Foot Ankle Int* 2008;29(7):671-6.

67. Di Caprio F, Buda R, Mosca M, et al. Foot and lower limb diseases in runners: assessment of risk factors. *J Sports Sci Med* 2010;9(4):587-96.

68. Milgrom C, Finestone A, Zin D, et al. Cold weather training: a risk factor for Achilles paratendinitis among recruits. *Foot Ankle Int* 2003;24(5):398-401.

69. van der Vlist AC, Breda SJ, Oei EHG, et al. Clinical risk factors for Achilles tendinopathy: a systematic review. *Br J Sports Med* 2019;53(21):1352-61.

70. O'Neill S, Watson PJ, Barry S. A Delphi study of risk factors for Achilles tendinopathy - opinions of world tendon experts. *Int J Sports Phys Ther.* 2016;11(5):684-97.

71. Blazina ME, Kerlan RK, Jobe FW, et al. Jumper's knee. *Orthop Clin North Am* 1973;4(3):665-78.

72. Plinsinga ML, van Wilgen CP, Brink MS, et al. Patellar and Achilles tendinopathies are predominantly peripheral pain states: a blinded case control study of somatosensory and psychological profiles. *Br J Sports Med* 2018;52(5):284-91.

73. Rio E, Moseley L, Purdam C, et al. The pain of tendinopathy: physiological or pathophysiological? *Sports Med* 2014;44(1):9-23.

74. Tompra N, van Dieen JH, Coppieters MW. Central pain processing is altered in people with Achilles tendinopathy. *Br J Sports Med* 2016;50(16):1004-7.

75. Hutchison AM, Evans R, Bodger O, et al. What is the best clinical test for Achilles tendinopathy? *Foot Ankle Surg* 2013;19(2):112-17.

76. Cook JL, Khan KM, Kiss ZS, et al. Reproducibility and clinical utility of tendon palpation to detect patellar tendinopathy in young basketball players. Victorian Institute of Sport tendon study group. *Br J Sports Med* 2001;35(1):65-9.

77. Reiman M, Burgi C, Strube E, et al. The utility of clinical measures for the diagnosis of Achilles tendon injuries: a systematic review with meta-analysis. *J Athl Train* 2014;49(6):820-9.

78. Mallows A, Littlewood C, Malliaras P. Measuring patient-reported outcomes (PROs/PROMs) in people with Achilles tendinopathy: how useful is the VISA-A? *Br J Sports Med* 2018;52(19):1221.

79. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

80. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: new treatment options. *Br J Sports Med* 2007;41(4):211-16.

81. Docking SI, Ooi CC, Connell D. Tendinopathy: is imaging telling us the entire story? *J Orthop Sports Phys Ther* 2015;45(11):842-52.

82. Cook J, Purdam CR. The challenge of managing tendinopathy in competing athletes. *Br J Sports Med* 2014;48(7):506-9.

83. Martin RL, Chimenti R, Cuddeford T, et al. Achilles pain, stiffness, and muscle power deficits: midportion Achilles tendinopathy revision 2018. *J Orthop Sports Phys Ther* 2018;48(5):A1-A38.

84. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: a randomized controlled trial. *Am J Sports Med* 2007;35(3):374-83.

85. Tumilty S, McDonough S, Hurley DA, et al. Clinical effectiveness of low-level laser therapy as an adjunct to eccentric exercise for the treatment of Achilles' tendinopathy: a randomized controlled trial. *Arch Phys Med Rehabil* 2012;93(5):733-9.

86. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41(7):e1-e6.

87. Wilson F, Walshe M, O'Dwyer T, et al. Exercise, orthoses and splinting for treating Achilles tendinopathy: a systematic review with meta-analysis. *Br J Sports Med* 2018;52(24):1564-74.

88. Joseph MF, Taft K, Moskwa M, et al. Deep friction massage to treat tendinopathy: A systematic review of a classic treatment in the face of a new paradigm of understanding. *J Sport Rehabil* 2012;21(4):343-53.

89. Fallon K, Purdam C, Cook J, et al. A "polypill" for acute tendon pain in athletes with tendinopathy? *J Sci Med Sport* 2008;11(3):235-8.

90. Vallone G, Vittorio T. Complete Achilles tendon rupture after local infiltration of corticosteroids in the treatment of deep retrocalcaneal bursitis. *J Ultrasound* 2014;17(2):165-7.

91. Taneja AK, Santos DC. Steroid-induced Kager's fat pad atrophy. *Skeletal Radiol* 2014;43(8):1161-4.

92. Hart L. Corticosteroid and other injections in the management of tendinopathies: a review. *Clin J Sport Med* 2011;21(6):540-41.

93. Ebbesen BH, Molgaard CM, Olesen JL, et al. No beneficial effect of Polidocanol treatment in Achilles tendinopathy: a randomised controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2018;26(7):2038-44.

94. Maffulli N, Spiezia F, Longo UG, et al. High volume image guided injections for the management of chronic tendinopathy of the main body of the Achilles tendon. *Phys Ther Sport* 2013;14(3):163-7.

95. de Vos RJ, Weir A, Tol JL, et al. No effects of PRP on ultrasonographic tendon structure and neovascularisation in chronic midportion Achilles tendinopathy. *Br J Sports Med* 2011;45(5):387-92.

96. Kearney Rebecca S, Parsons N, Metcalfe D, et al. Injection therapies for Achilles tendinopathy. *Cochrane Database Syst Rev* 2015;26(5):CD010960.

97. Liu CJ, Yu KL, Bai JB, et al. Platelet-rich plasma injection for the treatment of chronic Achilles tendinopathy: A meta-analysis. *Medicine (Baltimore)* 2019;98(16):e15278.

98. Cardoso TB, Pizzari T, Kinsella R, et al. Current trends in tendinopathy management. *Best Pract Res Clin Rheumatol* 2019;33(1):122-40.

99. Silbernagel KG, Thomeé R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35(6):897-906.

100. Cook JL. Ten treatments to avoid in patients with lower limb tendon pain. *Br J Sports Med* 2018;52(14):882

101. Stanish WD, Rubinovich RM, Curwin S. Eccentric exercise in chronic tendinitis. *Clin Orthop Relat Res* 1986(208):65-8.

102. Alfredson H, Pietilä T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26(3):360-6.

103. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9(1):42-7.

104. Fahlström M, Jonsson P, Lorentzon R, et al. Chronic Achilles tendon pain treated with eccentric calf-muscle training. *Knee Surg Sports Traumatol Arthrosc* 2003;11(5):327-33.

105. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2009;37(3):463-70.

106. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis a randomised trial. *Br J Sports Med* 2011;45(5):421-8.

107. Meyer A, Tumilty S, Baxter GD. Eccentric exercise protocols for chronic non-insertional Achilles tendinopathy: how much is enough? *Scand J Med Sci Sports* 2009;19(5):609-15.

108. Stevens M, Tan CW. Effectiveness of the Alfredson protocol compared with a lower repetition-volume protocol for midportion Achilles tendinopathy: a randomized controlled trial *J Orthop Sports Phys Ther* 2014;44(2):59-67.

109. Knobloch K, Schreibmueller L, Kraemer R, et al. Gender and eccentric training in Achilles mid-portion tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2010;18(5):648-55.

110. Sayana M, Maffulli N. Eccentric calf muscle training in non-athletic patients with Achilles tendinopathy. *J Sci Med Sport* 2007;10(1):52-8.

111. Silbernagel KG, Thomee R, Thomee P, et al. Eccentric overload training for patients with chronic Achilles tendon pain--a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports* 2001;11(4):197-206.

112. Beyer R, Kongsgaard M, Hougs Kjaer B, et al. Heavy slow resistance versus eccentric training as treatment for Achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2015;43(7):1704-11.

113. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes: a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.

114. Kountouris A, Cook J. Rehabilitation of Achilles and patellar tendinopathies. *Best Pract Res Clin Rheumatol* 2007;21(2):295-316.

CHAPTER 2

Eccentric exercise training in chronic mid-portion Achilles tendinopathy: a systematic review on different protocols

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ABSTRACT

Although eccentric exercise training has shown favorable results in chronic mid-portion Achilles tendinopathy (AT), the optimum dosage remains unknown. A systematic review of the literature was performed in accordance with the PRISMA guidelines, in order to describe different exercise protocols and to determine the most effective training parameters. An extensive search in MEDLINE, EMBASE, CINAHL, and CENTRAL revealed 14 randomised and clinical controlled trials. Strong evidence was found for the Alfredson exercise protocol. In this 12-week protocol, exercises are performed 3x15 repetitions twice daily, both with a straight and bent knee. Exercises are performed at slow speed, and load is increased when exercises are without pain. Strong evidence was also found for gradual onset of exercises during the first week of the Alfredson programme, but no uniformity of protocols exists. Other exercise protocols did achieve similar results, but many studies had some methodological shortcomings or lacked a detailed description of their training parameters.
Because of the heterogeneity of study populations and outcome measures, and lack of reporting of training compliance data, a definitive conclusion regarding the most effective training parameters could not be made. Further research comparing the content of different exercise protocols is warranted.

INTRODUCTION

Achilles tendinopathy (AT) is a common injury of the lower extremity, most prevalent in middle-aged men (35-45 years of age).[1 2] Although AT is often a result of overuse in sports involving running and jumping, up to one third of the patients has a sedentary lifestyle.[3]

Most ATs are localized 2-7 cm proximal to the calcaneal insertion (mid-portion),[4 5] which may be due to the relative hypovascularity in this region.[6] Insertional tendinopathy is considered a different entity, with a different injury mechanism,[7] and often much more recalcitrant to conventional treatment strategies.[5] The term tendinopathy was proposed by Maffulli et al. in 1998, in order to describe the clinical symptoms of pain, swelling, and impaired physical function.[8] Although traditionally considered as an inflammatory condition, research on histopathology has indicated that mid-portion AT is rather a result of a failed healing response that causes degenerative changes of the tendon.[3 9 10] Recently, tendinopathy has been described as a continuum, with three different stages (reactive tendinopathy, tendon disrepair, and degenerative tendinopathy).[10]
While tendon degeneration may particularly imply disordering of the normal collagen structure, it also concerns vasculo-neural ingrowth from the paratenon into the tendon.[11 12] Pain, as the primary symptom of AT, is considered a consequence of this neovascularization and nerve ingrowth.[3 13 14] However, besides these local tissue changes, peripheral and central nociceptive mechanisms might also be involved.[15] Yet, the exact mechanism needs to be further clarified.

Conservative treatment is usually the preferred choice in treatment of AT, at least for a period of 3-6 months.[3 4 16] Although a considerable amount of physiotherapeutic modalities are used, scientific evidence for many of them is limited.[17] Recent studies have shown evidence for eccentric exercise training (EET) of the lower leg for clinical outcomes such as pain, function, and return to work/sport.[16 18-20]

Many studies on EET in AT are based on the study of Alfredson et al. (1998), in which patients had to perform an eccentric heel-drop on the affected leg, and use the non-affected leg to (concentrically) return to the start position.[21] The exercise was performed three sets of 15 repetitions, twice daily (3x15 with the knee straight and 3x15 with the knee bent), for a period of 12 weeks. Load was increased guided by pain during the exercises. Although the authors reported significant decrease of pain and increased plantar flexor strength, the protocol that they used was based on clinical experience, and lacks a scientific basis.[22] As a consequence, different training protocols have originated, and the optimum dosage for EET remains unclear. Therefore, the aim of this study is to systematically review different EET protocols of the lower leg, and to investigate which training parameters are most effective for pain and patient-reported function in patients with mid-portion AT.

MATERIALS AND METHODS

A systematic review of the literature was performed in accordance with the PRISMA guidelines.[23]

Literature search

The electronic databases MEDLINE, EMBASE, CINAHL, and Cochrane Central Register for Controlled Trials (CENTRAL) were searched for relevant studies from their inception up to February 2013. A sensitive search strategy to identify controlled trials was applied,[24] in combination with the following keywords: Achilles tendon, tendinopathy, tendinosis, tendinitis, tendon injuries, exercise therapy, eccentric training, concentric training, and resistance training. A detailed description of the MEDLINE search is shown in Appendix 2.1. The search strategy was adapted for the other databases.

The electronic search was complemented by reference tracking of the included studies, and of four previous systematic reviews on therapeutic interventions for AT,[16 18 20 25] to make sure that no relevant studies were missed.

Eligibility criteria

Studies were eligible if they were randomised controlled trials (RCTs) or clinical controlled trials (CCTs) evaluating the effect of EET for patients with chronic mid-portion AT. At least one treatment group should have performed EET as a single intervention. Studies that only investigated concentric or combined concentric-eccentric exercise regimes were not included.

Subjects had to be over 18 years of age, and the mean duration of symptoms should be ≥ 3 months. All eligible studies must have been published in peer-reviewed journals. To prevent language bias, no language restrictions were imposed. Reviews, cohort studies, and case reports were excluded, as were studies on ruptures of the Achilles tendon. Surgical interventions were excluded unless surgery was used as a control intervention to compare to EET. A detailed description of the eligibility criteria is given in Table 2.1.

Study selection

After duplicates were removed, three reviewers (BH, RvC, NE) independently screened titles and abstracts for potential eligible studies. If title and abstract suggested that a study was eligible, a full text copy of the article was obtained. If no full text was available, the first author of the respective study was electronically contacted to retrieve a copy.

Disagreements of study selection between the three reviewers were resolved during a consensus meeting. The reviewers were not blinded to authors or journal of publication.

Table 2.1 Inclusion and exclusion criteria for selection of studies

Inclusion	Exclusion
Randomised controlled trials or clinical controlled trials	Prospective cohort studies, retrospective cohort studies, case reports/studies
Mid-portion Achilles tendinopathy	Location of tendinopathy unknown, or insertional tendinopathy
Chronic symptoms (mean duration of symptoms ≥ 3 months)	Comorbidities such as retrocalcaneal bursitis, superficial calcaneal bursitis, Haglund's syndrome, or rheumatological/vascular diseases
Adults (mean age ≥ 18 years)	Studies investigating concentric and/or concentric-eccentric exercise training as a single intervention
At least one group performing eccentric exercise training of the lower leg training as a single intervention	Studies on ruptured Achilles tendon
Published in peer-reviewed journal	Studies on surgery of the Achilles tendon (studies that used surgery as a control intervention to training were included)
	No outcome data reported for pain or physical function
	Review papers without original data
	Follow-up studies using previously reported data
	Studies without outcome data (e.g. study protocols, commentaries, expert opinions)
	Animal studies

Methodological quality assessment

To assess the methodological quality of the included studies, the PEDro score (www.pedro.org.au) was used, which has been shown to be sufficiently reliable for use in systematic reviews.[26] The scale consists of 11 criteria, of which the first is not included in the total score. Each criterion is rated 'yes' or 'no', and a 'yes' should only be awarded when a criterion is clearly satisfied. The maximum score that can be given is 10 if all criteria are satisfied. Three reviewers (BH, RvC, NE) independently assessed the methodological quality, and discrepancies were resolved by discussion until consensus was reached.

Risk of bias

To evaluate whether the results of the included studies are valid, risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias.[24]

Data extraction

Data extraction was performed by the first reviewer (BH), using a standard extraction form. Relevant data included: 1) author and year, 2) study design, 3) study participants, 4) type of intervention and training parameters (duration, sets/repetitions, frequency, speed, rate of progression, pain allowed during exercises?), 5) outcome measures, 6) results, 7) com-

pliance, and 8) concurrent sport activities. Outcome measures were restricted to pain and patient-reported function, as these are important clinical outcomes. If possible, follow-up periods were chosen directly after the intervention, so that bias due to other interventions or time would be minimized. When data were missing or further information was needed, serious efforts were made to contact the corresponding author of the respective study to request the required information.

Levels of evidence

Levels of evidence were interpreted using the classification of Van Tulder et al. (Table 2.2).[27] Included studies with a PEDro score of ≥6/10 were considered of high quality, whereas a score of 5/10 or lower was considered as low methodological quality.[22]

Table 2.2 Levels of evidence according to Van Tulder et al.[27]

Evidence	Criteria
Strong	Consistent findings in > 2 high quality studies
Moderate	Consistent findings in multiple lower-quality studies and/or one high-quality study
Limited	Only one relevant low-quality study
Conflicting	Inconsistent findings among multiple studies
No evidence from trials	No randomised controlled trials or clinical controlled trials available

RESULTS

Study selection

The process of identifying studies is shown in Figure 2.1. The initial search strategy identified 179 studies, of which 92 were left after removing duplicates. Based on their title and abstract, 72 studies were excluded. After applying inclusion and exclusion criteria for full-text versions, 12 studies were left to be included. One study could not be obtained in full text despite a request to the authors, and was therefore not included in the review. Reference tracking identified two additional studies.[21 28]

A final search performed in September 2013 revealed one potential new study.[29] However, this study was excluded as the location of tendinopathy was not described.

Methodological quality assessment

Initial agreement (kappa) between the reviewers concerning methodological quality was substantial (κ = 0.723) Table 2.3 shows the methodological quality scores of the included studies after the consensus meeting. Quality assessment yielded six studies (43%) of high methodological quality.[30-35] Three studies (21%) were CCTs,[21 28 36] the remainder were

RCTs.[30-35 37-41] Only five studies (36%) clearly described concealment of allocation.[31-35] None of the studies did satisfy the criteria regarding blinding of subjects and therapists. Blinding of the outcome assessors was satisfied in 43% of the studies.[30 32 33 35 36 38] Nine studies (64%) mentioned either the use of intention-to-treat data analysis,[31-35] or explicitly reported that all subjects received the allocated intervention.[30 36 37 39]

Risk of bias

Results for risk of bias assessment are listed in Table 2.4. Risk of bias regarding the blinding of subjects and personnel was high in all studies, which corresponds to the PEDro scores for these items. Six studies (43%) had low risk of bias for incomplete outcome data.[28 30 33 35-37 39] In all other studies reasons for attrition were not clearly described or differed between groups, resulting in high risk of bias.

Study characteristics

The included studies investigated a total of 794 patients, of which less than 50% (i.e. 389 patients) received EET as a single intervention. Mean age ranged from 32.5-53.5 years, and included patients were both athletes and non-athletes. Table 2.5 provides an overview of all relevant study characteristics.

All studies that investigated EET protocols have reported significant improvement for the intervention groups, except for the study of Chester et al. (2008), who reported a deterioration in functional activities after their intervention.[37]

There were three studies that reported data on training compliance.[34 35 38] These studies reported good compliance (i.e. at least 75% of exercises performed) in 26.7-72% of the patients.

Because of the heterogeneity of study populations and outcome measures, statistical pooling of the data was not possible. Therefore, only a qualitative data synthesis was performed.

Exercise training protocols

Seven studies (50%),[21 28 33 35 36 38 39] of which three were high-quality studies,[33 35 36] have used the exact protocol as described by Alfredson and colleagues. In this protocol, patients performed 3x15 repetitions twice daily, for a period of 12 weeks. Exercises were performed with both straight and bent knee, and non-disabling pain was allowed during the exercises. Load was increased when exercises could be performed without discomfort, but only Rompe et al. described the amount of weight that was added (5 kg).[33]

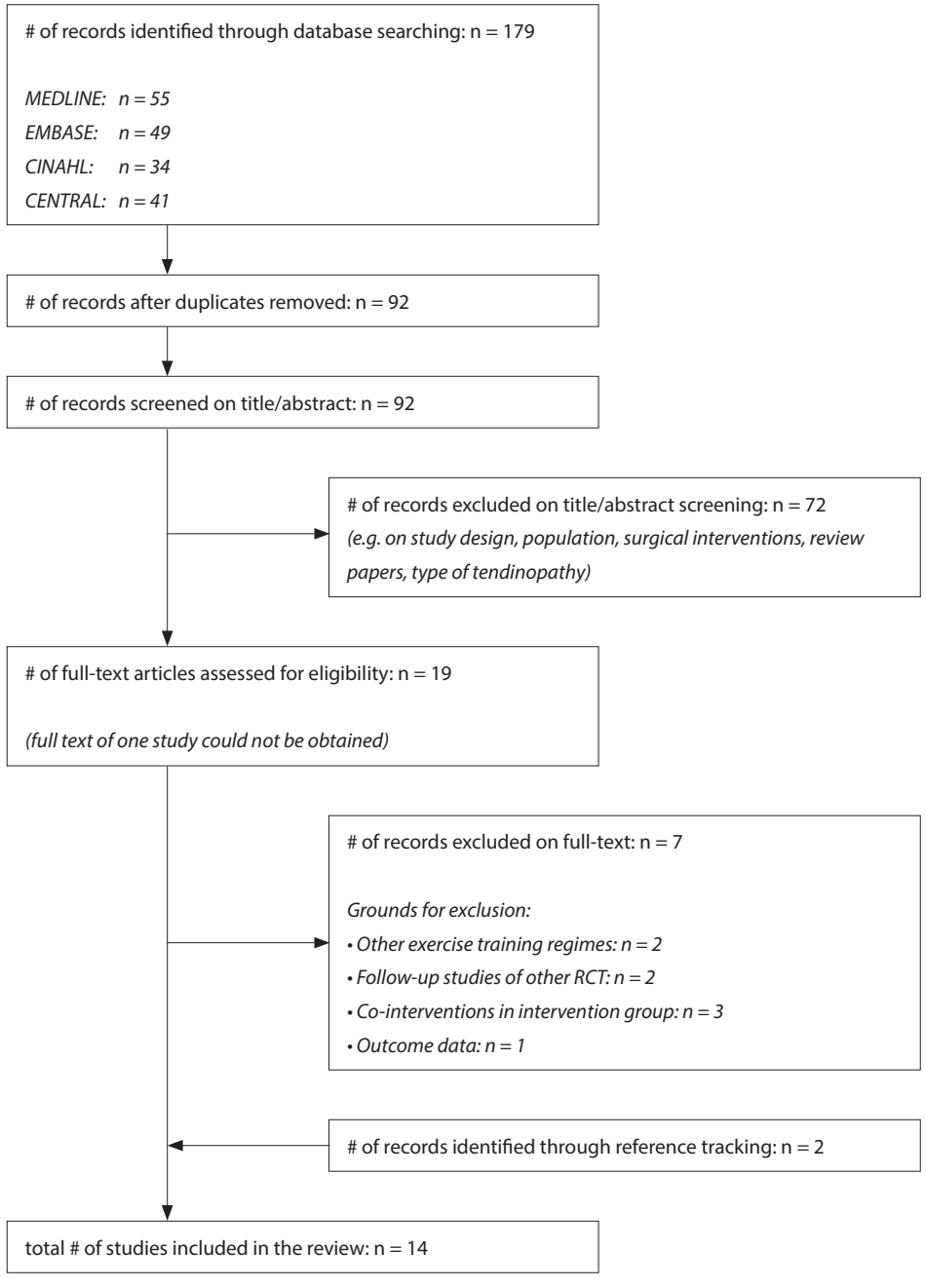

Figure 2.1 Flow chart of the search strategy

Table 2.3 Methodological quality assessment of the included studies

	Criteria											
Study (year)[a]	1[b]	2	3	4	5	6	7	8	9	10	11	Total score
Rompe (2007)	+	+	+	+	-	-	+	+	+	+	+	8/10
Rompe (2009)	+	+	+	+	-	-	+	+	+	+	+	8/10
Yelland (2011)	+	+	+	-	-	-	+	+	+	+	+	7/10
Knobloch (2007)	+	+	-	+	-	-	+	+	+	-	+	6/10
Knobloch (2008)	+	+	+	+	-	-	-	-	+	+	+	6/10
Roos (2004)	+	+	+	+	-	-	-	-	+	+	+	6/10
Stasinopoulos (2012)	+	-	-	+	-	-	+	+	+	+	+	6/10
Chester (2008)	+	+	-	-	-	-	-	+	+	+	+	5/10
De Vos (2007)	+	+	-	+	-	-	+	+	-	+	-	5/10
Mafi (2001)	+	+	-	+	-	-	-	+	+	+	-	5/10
Petersen (2007)	+	+	-	+	-	-	-	+	-	+	+	5/10
Nørregaard (2007)	+	+	-	+	-	-	-	-	-	+	-	3/10
Fahlström (2003)	-	-	-	-	-	-	-	+	-	-	+	2/10
Alfredson (1998)	-	-	-	-	-	-	-	-	-	-	+	1/10

+ indicates that a criterion was satisfied; - indicates that a criterion was not satisfied
1: eligibility criteria described?; *2:* random allocation?; *3:* allocation concealed?;
4: group similarity at baseline?; *5:* subjects blinded?; *6:* therapists blinded?;
7: outcome assessors blinded?; *8:* adequate follow-up?; *9:* intention-to-treat analysis?;
10: between-group comparison?; *11:* point measures and measures of variability?
[a] Studies are listed in descending order of methodological quality
[b] This criterion is not used in the calculation of the total score

There were two studies (14%),[32 34] both of high methodological quality, that used a protocol nearly similar to the Alfredson protocol, but with a gradual onset of exercises during the first week. In the study of Rompe et al. (2007), patients started with one set of 10 repetitions on the first day, and progressed to three sets of 15 repetitions once daily on the seventh day.[32] From week 2, exercises were performed twice daily, similar to the original Alfredson protocol, and load was increased with 5 kg guided by pain. Roos et al. (2004), on the other hand, prescribed 1x15 repetitions on the first two days (with extended knee), progressing to 2x15 on the third and fourth day, and three sets of 15 repetitions on days 5-7.[34] During weeks 2-12, exercises were performed twice daily, with both extended and bent knee. Although they reported that weight was increased during the intervention period, these authors did not provide information on the amount of weight that was added.

Besides the aforementioned protocols, several other protocols that used different training parameters, were used. Petersen et al. (2007) used a protocol similar to the Alfredson protocol,[41] but in their study, exercises were performed thrice daily. Furthermore, one study used a protocol that consisted of 1x15 repetitions with an extended knee, and 1x15 with a bent

knee.[40] If possible, a second and third set were repeated, and once pain decreased, weight was added in a backpack (5 kg). In the studies of Knobloch et al.,[30 31] both of high methodological quality, different protocols were used: in one study patients performed 3x15 repetitions once daily,[30] while in the other exercises were performed twice daily.[31] The position of the knee was not described in both studies. Finally, Chester et al. (2008) used a protocol in which patients performed up to three sets of 15 repetitions with an extended knee.[37] If pain and strength allowed, also three sets with a bent knee were performed. In contrast with other protocols, Chester et al. (2008) described a 10 s static hold in the lowest position (dorsiflexion), before concentrically returning to the starting position with the uninjured leg. Progression was made by either increasing the number of repetitions or the amount of weight.

Table 2.4 Risk of bias assessment of the included studies

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessments	Incomplete outcome data	Selective reporting
Rompe (2007)	+	+	-	+	+	?
Rompe (2009)	+	+	-	+	-	?
Yelland (2011)	+	+	-	+	+	?
Knobloch (2007)	?	?	-	+	+	?
Knobloch (2008)	+	+	-	-	-	?
Roos (2004)	?	?	-	+	?	?
Stasinopoulos (2012)	-	-	-	+	+	+
Chester (2008)	+	?	-	-	-	?
De Vos (2007)	?	?	-	+	-	?
Mafi (2001)	+	?	-	?	+	-
Petersen (2007)	+	-	-	?	?	?
Nørregaard (2007)	+	?	-	-	-	?
Fahlström (2003)	-	-	-	?	+	?
Alfredson (1998)	-	-	-	?	?	?

+ = low risk of bias; - = high risk of bias; *?* = unclear risk of bias

Levels of evidence

Strong evidence was found for the original Alfredson eccentric protocol from three high-quality studies.[33 35 36] There was also strong evidence from two high-quality studies to support the use of a gradual onset of exercises during the first week,[32 34] but no uniformity in protocols exists. Moderate evidence was found for the different protocols that were used in other studies.[30 31 37]

DISCUSSION

The aim of this study was to systematically review different EET protocols of the lower leg, and to investigate which training parameters were most effective for pain and patient-reported function. Six out of 13 included studies used the protocol that was originally described by Alfredson et al. (1998). In the Alfredson protocol patients performed 3x15 repetitions twice daily, with both a straight and bent knee. Exercises were performed seven days per week, for a period of 12 weeks. Non-disabling pain was allowed during exercises, and once exercises could be performed without pain, load was increased by adding weight. However, only one study explicitly mentioned the amount of weight that was used (5 kg).[33] Furthermore, information on the speed at which the exercises should be performed is lacking in all studies. Alfredson and colleagues stated that exercises were performed at slow speed,[21] but further details were not provided. All studies that used the Alfredson protocol found significant improvement for both pain and function. Although the outcome measures differed between studies, four studies used the Victorian Institute of Sport Assessment – Achilles (VISA-A) score,[33 35 36 38] which is frequently recommended for use in AT research.[42 43] These studies reported an increase of the VISA-A score following intervention ranging from 37-111%.

Although the Alfredson protocol resulted in significant improvement of pain and function, other protocols did achieve similar results. Two studies investigated a protocol that was nearly similar to the Alfredson protocol, but with a gradual onset of exercises during the first week. In the study of Rompe et al. (2007), patients performed 1x10 repetitions on the first day and progressed to 3x15 repetitions once daily on the seventh day.[32] From weeks 2-12 they continued according to the Alfredson programme.

Rompe et al. (2007) did not describe the knee position during the first exercise week. They used the VISA-A score as their primary outcome measure, which was also used in the aforementioned studies that used the original Alfredson protocol.[33 35 36 38] While Rompe et al. (2007) reported an improvement of 49% at 16 week follow-up, the studies that used the original Alfredson protocol reported percentages ranging from 37-111%. In the study of Roos et al. (2004), gradual onset of exercises started with 1x15 on the first two days, progressing to 2x15 on days 3-4 and 3x15 on days 5-7.[34] During the first week, exercises were performed only with the knee extended, and patients continued with the original Alfredson programme from weeks 2-12. Although the authors reported significant improvement following their intervention, comparison to other studies is difficult as they used a different outcome measure (Foot and Ankle Outcome Score). Therefore, whether a gradual onset of exercises in the first week is of additional value remains unclear, although it might prevent muscle soreness in the first week.[34]

Table 2.5 Overview of relevant characteristics and results of the included studies

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Rompe (2007)	RCT	n = 75; 46 women, 29 men; mean age 48.6 years; A: 25 B: 25 C: 25	A: eccentric training B: shock-wave therapy C: control group; wait-and-see	- 12 weeks - 3x15 repetitions (start with 1x10 on first day and gradually increase to 3x15 in second week) - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - add 5kg when exercises could be completed with no pain - pain allowed	VISA-A NRS for pain during the day (16 weeks)	VISA-A from 50.6±11.5 to 75.6±18.7 ($P < .05$) NRS from 7.0±0.8 to 3.6±2.3 ($P < .05$)	Compliance: not reported Sport activities: allowed after 4 weeks
Rompe (2009)	RCT	n = 68; 38 women, 30 men; mean age 49.7 years; A: 34 B: 34	A: eccentric training B: eccentric training + shockwave therapy	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - add 5 kg when exercises were not painful - pain allowed	VISA-A NRS for pain during the day (16 weeks)	VISA-A from 51±10 to 73±19 ($P < .05$) NRS from 7.0±0.8 to 3.9±2.0 ($P < .05$)	Compliance: not reported Sport activities: no sport during intervention period

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Yelland (2011)	RCT	n = 43; sex not reported; median age 46.7 years; A: 15 B: 14 C: 14	A: eccentric training B: prolotherapy injections C: eccentric training + prolotherapy injections	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - add load as the pain eases over time - pain allowed	VISA-A NRS for worst pain in last week NRS for limitation of usual activities (3 months)	VISA-A from 57.7±14.2 to 80.4±15.4 ($P < .05$) NRS: data are graphically reported and could therefore not be extracted	Compliance: at 12 weeks 27% reported good compliance (> 75%) Sport activities: not reported
Knobloch (2007)	RCT	n = 20; 9 women, 11 men; mean age 32.5 years; A: 5 B: 15	A: control group; repetitive cryotherapy B: eccentric training	- 12 weeks - 3x15 repetitions - once daily - speed: 2 sec for both concentric and eccentric part - rate of progression unknown - pain: not reported	VAS for pain (12 weeks)	VAS from 4.1±2.9 to 2.1±2.2 ($P < .05$)	Compliance: not reported Sport activities: allowed during intervention period
Knobloch (2008)	RCT	n = 97; 34 women, 63 men; mean age 47.5 years; A: 43 B: 54	A: eccentric training + AirHeel brace B: eccentric training	- 12 weeks - 3x15 repetitions - twice daily - speed unknown - rate of progression unknown - pain allowed	VAS for pain FAOS (12 weeks)	FAOS - symptoms: from 69±17 to 75±18 ($P < .05$) - pain: from 69±19 to 81±19 ($P < .05$) - sport: from 67±23 to 78±21 ($P < .05$) VAS from 5.4 ± 2.1 to 3.6 ± 2.4 ($P < .05$)	Compliance: not reported Sport activities: allowed during intervention period

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Roos (2004)	RCT	n = 44; 23 women, 21 men; mean age 46 years; A: 16 B: 15 C: 13	A: eccentric training B: eccentric training + night splint C: night splint	- 12 weeks - 3x15 repetitions (gradual onset during first week: days 1-2: 1x15, days 3-4: 2x15, days 5-7: 3x15) - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - add weight when exercises were without discomfort - pain allowed	FAOS Physical activity level on 7-point scale (12 weeks)	FAOS - symptoms: from 61±12 to 79±19 ($P < .05$) - pain: from 60±19 to 82±18 ($P < .05$) - sport: from 42±23 to 74±20 ($P < .05$) Physical activity: 5/8 patients returned to pre-injury activity level	Compliance: at 12 weeks 50% reported good compliance (> 75%) Sport activities: not reported
Stasinopoulos (2012)	CCT	n = 41; sex not reported; mean age 48.3 years; A: 21 B: 20	A: concentric-eccentric training (Stanish protocol) B: eccentric training (Alfredson protocol)	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee; 1x with bent knee) - slow speed - increase load when exercises could be performed without any minor pain or discomfort - pain allowed	VISA-A (12 weeks)	VISA-A: from 36 to 76 ($P < .05$) Significant between-group difference in favor of group B	Compliance: not reported Sport activities: not allowed during intervention period

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Chester (2008)	RCT	n = 16; 5 women, 11 men; mean age 53.5 years; A: 8 B: 8	A: eccentric training B: ultrasound	- 12 weeks - 3x15 repetitions (adjusted to subjects' physical ability/pain) - once daily with straight knee (and once daily with bent knee if pain/strength allowed) - speed: 10 sec hold in end positions - increased number or weight when exercise pain had settled - pain allowed	VAS for pain 1. during walking 2. during rest 3. after sports/recreation FILLA (12 weeks)	VAS 1. from 50.5±33.4 to 48.5±23.4 2. from 36.3±30.8 to 26.6±25.9 3. from 70.0±19.2 to 61.9±23.5 FILLA from 45.2±22.6 to 53.0±17.6	Compliance: not reported Sport activities: not reported
De Vos (2007)	RCT	n = 63; 26 women, 37 men; mean age 44.6 years; A: 32 B: 31	A: eccentric training B: eccentric training + night splint	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - increase load when exercises could be performed without discomfort - pain allowed	VISA-A (12 weeks)	VISA-A from 50.1 to 68.8 ($P < .05$)	Compliance: at 12 weeks 72% reported good compliance (> 50%) Sport activities: allowed after 4 weeks

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Mafi (2001)	RCT	n =44; 20 women, 24 men; mean age 48 years; A: 22 B: 22	A: eccentric training B: concentric training	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee; 1x with bent knee) - speed unknown - increase load when exercises could be performed without any minor pain or discomfort - pain allowed	VAS for pain during walking/running (12 weeks)	VAS from 69 to 12 Between-group difference not reported	Compliance: not reported Sport activities: allowed during intervention period
Petersen (2007)	RCT	n = 100; 40 women, 60 men; mean age 42.5 years; A: 37 B: 35 C: 28	A: eccentric training B: Airheel brace C: eccentric training + Airheel brace	- 12 weeks - 3x15 repetitions - three times daily (with straight knee and with bent knee) - speed unknown - increase load when exercises could be performed without any minor pain or discomfort - pain allowed	VAS for pain 1. during ADLs 2. during walking 3. during sports AOFAS scale (12 weeks)	VAS: data are graphically reported and could therefore not be extracted (pain reduction ranged from 51-71%, $P < .05$)) AOFAS scale: data are graphically reported and could therefore not be extracted	Compliance: not reported Sport activities: allowed during intervention period

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Nørregaard (2007)	RCT	n = 45[c]; sex not reported; mean age 42 years;	A: eccentric training B: control group; stretching	- 12 weeks - 1x15 repetitions, increasing to 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - speed unknown - add 5kg when pain decreased - pain allowed	Questionnaire on self-reported symptoms (12 weeks)	Baseline scores not reported, and change scores could therefore not be extracted (significant improvement within-group, $P < .05$)	Compliance: data were registered, but not reported Sport activities: allowed during intervention period
Fahlström (2003)	CCT	n = 108; 31 women, 77 men; mean age 42 years; A: 78 B: 30[d]	A: eccentric training B: eccentric training	A + B: - 12 weeks - 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - slow speed - add weight when exercises could be performed without any minor pain or discomfort - pain allowed	VAS for pain during walking / jogging / running (12 weeks)	VAS from 66.8±19.4 to 10.2±13.7 in subjects who were satisfied ($P < .05$) VAS from 74.0±18.9 to 64.9±26.4 in subjects who were not satisfied	Compliance: not reported Sport activities: allowed after 4 weeks

Table 2.5 (Continued)

Study (year)	Study design	Sample (n)	Intervention	Training parameters[a]	Relevant outcome measures (follow-up)	Results (*P*-value)[b]	Compliance data and concurrent sport activities
Alfredson (1998)	CCT	n = 30; 7 women, 23 men; mean age 42 years; A: 15 B: 15	A: eccentric training B: surgery	- 12 weeks - 3x15 repetitions - twice daily (1x with straight knee, 1x with bent knee) - slow speed - add weight when exercises could be performed without any minor pain or discomfort - pain allowed	VAS for pain during running (12 weeks)	VAS from 81.2±18.0 to 4.8±6.5 ($P < .05$)	Compliance: not reported Sport activities: allowed during intervention period

RCT = randomised controlled trial; *CCT* = clinical controlled trial; *VISA-A* = Victorian institute for sport assessment-Achilles; *NRS* = numerical rating scale; *VAS* = visual analogue scale; *FAOS* = foot and ankle outcome score; *ADL* = activities of daily living; *AOFAS* = American orthopaedic foot and ankle society; *FILLA* = functional index of the leg and lower limb

[a] Duration of intervention; sets/repetitions; frequency; speed; rate of progression; pain allowed during exercises?

[b] Results are only reported for groups that performed eccentric exercise training as a single intervention

[c] Number of subjects randomised in each group at baseline not reported

[d] Group consisted of subjects with insertional tendinopathy

There were few studies that used different eccentric training protocols. Petersen et al. (2007) prescribed the Alfredson eccentric exercises thrice daily in their study,[41] and they reported significant reduction of pain and improvement of function as measured with the visual analog scale and the American Orthopaedic Foot and Ankle Society (AOFAS) score. However, the study of Petersen et al. (2007) had some methodological shortcomings (e.g. no allocation concealment, assessors not blinded, no intention-to-treat analysis), which makes their results prone to possible bias. Furthermore, this was the only study that used the AOFAS as an outcome measure, which makes comparison with other protocols difficult. Knobloch et al. performed two studies to investigate the effects of eccentric training in comparison to either repetitive cryotherapy[30] or an Airheel brace.[31] Both studies were of high methodological quality, but they used different protocols. In one study the researchers used 3x15 with a frequency of once per day, and a 2-s speed for the eccentric phase.[30] Pain reduction was approximately 50%, but with a sample of 15 patients, this study was relatively underpowered. In their other study, exercises were performed twice daily, but the speed at which exercises were performed was not described.[31] In the latter study, pain reduction was less (33%), but sample size was more adequate (n = 54). For both studies, the authors did not describe the knee position during exercises, which makes reproducibility of their results difficult. Finally, Chester et al. (2008) also used a different 12-week exercise protocol: the amount of repetitions and sets was adjusted to the subject's ability and pain. Furthermore, they used a 10-s static hold in the lowest position, before concentrically returning to the start position. Their results showed no significant difference in pain compared to therapeutic ultrasound. Interestingly, there was even a decrease in functional activities for the EET group compared to baseline scores. However, given the relatively small sample size and methodological shortcomings, conclusions should be interpreted with caution.

This review has several limitations. Firstly, we chose to include all relevant studies that investigated EET. In this way, studies of poor methodological quality (i.e. PEDro score < 6) were also included. Although we might have chosen to include only high methodological studies with a PEDro score of ≥ 6/10, we felt that our method would give a more comprehensive overview of all protocols that were used. Secondly, one study was not included in our review, since it could not be obtained in full text. Information on the exercise regime used in this study might have influenced the results of our review. Thirdly, we chose to exclude the protocol that was described by Stanish et al. (1986),[44] which was used in one study.[36] Although the authors originally described it as an eccentric exercise protocol, the Stanish protocol actually involves both eccentric and concentric muscle contractions.

The results of our study correspond to previous reviews, showing strong evidence for EET.[16 20] However, these previous studies assessed the effects of eccentric training in general, and did not investigate the superiority of any protocol in terms of training parameters. In 2009, Meyer et al. (2009) performed a systematic review on the effectiveness of different dosages in eccentric exercise protocols.[25] Although no definitive recommendation could

be made, they concluded that there was a trend in favor of a less stringent protocol than the Alfredson protocol, but this was not further explained. Their conclusions were based on three high-quality RCTs, of which none used the original Alfredson protocol. Two of three studies were also included in the current review, and both used a gradual onset of exercises.[32 34] The third study by Herrington and McCulloch (2007) was excluded because subjects in the eccentric training group received deep friction massage, stretching, and ultrasound in addition to their training.[45] Their protocol consisted of a combination of the Alfredson and Stanish programme. Subjects performed three sets of 15 repetitions twice daily, with both straight and bent knee. However, instead of adding weight for progression, initially speed was increased from slow to fast when exercises were without discomfort. Once exercises could be performed without discomfort and at fast speed, further progression was made by adding load. Speed then again was increased from slow to fast. The authors reported a significant 51.8% improvement of VISA-A scores in the EET group, but sample size was relatively small (n = 13). Furthermore, there are no other studies that have used the same protocol.

While EET seems to be an effective treatment modality, it has been stated that up to 24-45% of the patients do not respond to EET.[1 3] This may be due to the fact that success rates depend on compliance. Of the three studies that reported compliance data,[34 35 38] good compliance (i.e. > 75% of the exercises performed) was found in 26-72% of the patients who returned their training logs. However, the majority of the included studies did not report any data on training compliance, which may have affected their results. Another possible underlying reason may be that the stage of tendinopathy as indicated by Cook and Purdam (2009) is not considered in many studies.[10] For example, if eccentric exercises are offered in the reactive stage, this potentially may further aggravate the tendon,[10] resulting in unsuccessful treatment. Additionally, it may be of importance for the effectiveness of EET if patients are allowed to perform their regular sport activities during the intervention. In our review, six studies reported that patients should perform their regular sport activities during the intervention,[21 30 31 39-41] whereas two studies allowed pain-free sport activities from weeks 4-6.[33 38] The other studies did not allow concurrent sport activities, or lacked detailed information.

In conclusion, our review could not reveal conclusive evidence regarding the effectiveness of different training parameters for EET protocols. Because of the heterogeneity in study populations and outcome measures, statistical pooling of the data was not possible. Furthermore, many studies did not report data on training compliance. Hence, the magnitude of the effects cannot be calculated, and a definitive conclusion is difficult to make. A scientific basis for the different training parameters that are used is lacking,[22] and no consensus exists on the exact histopathological response to EET.[46-49] There are no studies that have directly compared different EET protocols with different training parameters. Furthermore, no studies have compared EET to other exercise regimes, such as concentric EET, isometric training, or heavy slow resistance training (HSRT). The latter has shown

promising results in patellar tendinopathy,[50 51] but it has not yet been investigated in AT. Future studies should compare different protocols with different training parameters in order to determine which protocols are most effective. Uniformity of outcome measures is warranted in order to facilitate comparison between different protocols.

Perspectives

The present review aimed to describe several different EET protocols of the lower leg, and to investigate which training parameters are most effective for pain and function in patients with chronic mid-portion AT. Traditionally, the Alfredson protocol has been used in many studies, but our review showed that other protocols may achieve similar results.

Although most of the EET protocols have shown beneficial effects, scientific evidence for the training parameters that are used is lacking. Additionally, many studies lack detailed information on training parameters and training compliance. Because of the heterogeneity in study populations and outcome measures, there is no conclusive evidence regarding the most effective protocol. The findings of this study highlight the need for further research comparing the content of different eccentric exercise protocols. Furthermore, since EET is not beneficial for every patient, it is of interest to compare it to other training regimes, such as concentric-eccentric, isometric, or heavy slow resistance training,

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REFERENCES

1. Alfredson H, Lorentzon R. Chronic Achilles tendinosis: recommendations for treatment and prevention. *Sports Med* 2000;29(2):135-46.

2. Cook JL, Khan KM, Purdam C. Achilles tendinopathy. *Man Ther* 2002;7(3):121-30.

3. *Longo U, Ronga M, Maffulli N. Achilles tendinopathy. Sports Med Arthrosc Rev* 2009;17(2):112-26.

4. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: new treatment options. *Br J Sports Med* 2007;41(4):211-16.

5. van Dijk CN, van Sterkenburg MN, Wiegerinck JI, et al. Terminology for Achilles tendon related disorders. *Knee Surg Sports Traumatol Arthrosc* 2011;19(5):835-41.

6. Chen TM, Rozen WM, Pan WR, et al. The arterial anatomy of the Achilles tendon: anatomical study and clinical implications. *Clin Anat* 2009;22(3):377-85.

7. Cook J, Purdam C. Is compressive load a factor in the development of tendinopathy? *Br J Sports Med* 2012;46(3):163-68.

8. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. *Arthroscopy* 1998;14(8):840-43.

9. Abate M, Silbernagel KG, Siljeholm C, et al. Pathogenesis of tendinopathies: inflammation or degeneration? *Arthr Res Ther* 2009;11(3):235.

10. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. *Br J Sports Med* 2009;43(6):409-16.

11. Alfredson H. Chronic midportion Achilles tendinopathy: an update on research and treatment. *Clin Sports Med* 2003;22(4):727-41.

12. Khan KM, Cook JL, Bonar F, et al. Histopathology of common tendinopathies. Update and implications for clinical management. *Sports Med* 1999;27(6):393-408.

13. Zafar M, Mahmood A, Maffulli N. Basic science and clinical aspects of achilles tendinopathy. *Sports Med Arthrosc Rev* 2009;17(3):190-97.

14. van Sterkenburg M, van Dijk CN. Mid-portion Achilles tendinopathy: why painful? An evidence-based philosophy. *Knee Surg Sports Traumatol Arthrosc* 2011;19(8):1367-75.

15. Rio E, Moseley L, Purdam C, et al. The pain of tendinopathy: physiological or pathophysiological? *Sports Med* 2014;44(1):9-23.

16. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.

17. McLauchlan GJ, Handoll HH. Interventions for treating acute and chronic Achilles tendinitis. *Cochrane Database Syst Rev* 2001(2):CD000232.

18. Kingma JJ, de Knikker R, Wittink HM, et al. Eccentric overload training in patients with chronic Achilles tendinopathy: a systematic review. *Br J Sports Med* 2007;41(6):e3.

19. Magnussen RA, Dunn WR, Thomson AB. Nonoperative treatment of midportion Achilles tendinopathy: a systematic review. *Clin J Sport Med* 2009;19(1):54-64.

20. Sussmilch Leitch SP, Collins NJ, Bialocerkowski AE, et al. Physical therapies for Achilles tendinopathy: systematic review and meta-analysis. *J Foot Ankle Res* 2012;5(1):15.

21. Alfredson H, Pietilä T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26(3):360-66.

22. Woodley B, Newsham West R, Baxter GD. Chronic tendinopathy: effectiveness of eccentric exercise. *Br J Sports Med* 2007;41(4):188-98.

23. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62(10):1006-12.

24. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions Version 5.1.0 [updated March 2011]: *The Cochrane Collaboration* 2011.

25. Meyer A, Tumilty S, Baxter GD. Eccentric exercise protocols for chronic non-insertional Achilles tendinopathy: how much is enough? *Scand J Med Sci Sports* 2009;19(5):609-15.

26. Maher C, Sherrington C, Herbert R, et al. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther* 2003;83(8):713-21.

27. van Tulder M, Furlan A, Bombardier C, et al. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine (Philadelphia, Pa1976)* 2003;28(12):1290-99.

28. Fahlström M, Jonsson P, Lorentzon R, et al. Chronic Achilles tendon pain treated with eccentric calf-muscle training. *Knee Surg Sports Traumatol Arthrosc* 2003;11(5):327-33.

29. Yu JH, Park DS, Lee GC. Effect of eccentric strengthening on pain, muscle strength, endurance, and functional fitness factors in male patients with Achilles tendinopathy. *Am J Phys Med Rehabil* 2013;92(1):68-76.

30. Knobloch K, Kraemer R, Jagodzinski M, et al. Eccentric training decreases paratendon capillary blood flow and preserves paratendon oxygen saturation in chronic achilles tendinopathy. *J Orthop Sports Phys Ther* 2007;37(5):269-76.

31. Knobloch K, Schreibmueller L, Longo UG, et al. Eccentric exercises for the management of tendinopathy of the main body of the Achilles tendon with or without an AIRHEEL brace. A randomized controlled trial. B: effects of compliance. *Disabil Rehabil* 2008;30(20-22):1692-96.

32. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: A randomized controlled trial. *Am J Sports Med* 2007;35(3):374-83.

33. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2009;37(3):463-70.

34. Roos EM, Engstrom M, Lagerquist A, et al. Clinical improvement after 6 weeks of eccentric exercise in patients with mid-portion Achilles tendinopathy -- a randomized trial with 1-year follow-up. *Scand J Med Sci Sport*s 2004;14(5):286-95.

35. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med* 2011;45(5):421-28.

36. Stasinopoulos D, Manias P. Comparing two eccentric exercise programmes for the management of Achilles tendinopathy. A pilot trial. *J Bodyw Mov Ther* 2013;17(3):309-15.

37. Chester R, Costa ML, Shepstone L, et al. Eccentric calf muscle training compared with therapeutic ultrasound for chronic Achilles tendon pain - A pilot study. *Man Ther* 2008;13(6):484-91.

38. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41(7):e1-e6.

39. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9(1):42-47.

40. Nørregaard J, Larsen CC, Bieler T, et al. Eccentric exercise in treatment of Achilles tendinopathy. *Scand J Med Sci Sports* 2007;17(2):133-38.

41. Petersen W, Welp R, Rosenbaum D. Chronic Achilles tendinopathy: a prospective randomized study comparing the therapeutic effect of eccentric training, the AirHeel brace, and a combination of both. *Am J Sports Med* 2007;35(10):1659-67.

42. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

43. Scott A, Docking S, Vicenzino B, et al. Sports and exercise-related tendinopathies: a review of selected topical issues by participants of the second International Scientific Tendinopathy Symposium (ISTS) Vancouver 2012. *Br J Sports Med* 2013;47(9):536-44.

44. Stanish WD, Rubinovich RM, Curwin S. Eccentric exercise in chronic tendinitis. *Clin Orthop Relat Res* 1986(208):65-68.

45. Herrington L, McCulloch R. The role of eccentric training in the management of Achilles tendinopathy: A pilot study. *Phys Ther Sport* 2007;8(4):191-96.

46. Drew B, Smith T, Littlewood C, et al. Do structural changes (eg, collagen/matrix) explain the response to therapeutic exercises in tendinopathy: a systematic review. *Br J Sports Med* 2014;48(12):966-72.

47. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.

48. Ohberg L, Lorentzon R, Alfredson H. Eccentric training in patients with chronic Achilles tendinosis: Normalised tendon structure and decreased thickness at follow up. *Br J Sports Med* 2004;38(1):8-11.

49. Langberg H, Ellingsgaard H, Madsen T, et al. Eccentric rehabilitation exercise increases peritendinous type I collagen synthesis in humans with Achilles tendinosis. *Scand J Med Sci Sports* 2007;17(1):61-6.

50. Kongsgaard M, Qvortrup K, Larsen J, et al. Fibril morphology and tendon mechanical properties in patellar tendinopathy: effects of heavy slow resistance training. *Am J Sports Med* 2010;38(4):749-56.

51. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports* 2009;19(6):790-802.

SUPPLEMENTARY MATERIAL

Appendix 2.1 Search strategy for MEDLINE (Pubmed)

Population/problem of interest:

tendinopathy[Mesh]
tendinopathy[tiab]
tendinopathies[tiab]
tendonopathy[tiab]
tendonopathies[tiab]
tendinosis[tiab]
tendinoses[tiab]
tendonosis[tiab]
tendonoses[tiab]
tendinitis[tiab]
tendonitis[tiab]
tenosynovitis[Mesh]
tenosynovitis[tiab]
paratenonitis[tiab]
paratendinopathy[tiab]
paratendinopathies[tiab]
"soft tissue injuries"[Mesh]
"soft tissue injuries"[tiab]
"soft tissue injury"[tiab]
"tendon injuries"[Mesh]
"tendon injuries"[tiab]
"tendon injury"[tiab]
"neovascularization, pathologic"[Mesh]
neovascularization[tiab]
neovascularisation[tiab]

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"achilles tendons"[tiab]
"tendo achilles"[tiab]
tendoachilles[tiab]
tendo-achilles[tiab]
"tendo achillis"[tiab]
tendo-achillis[tiab]
tendoachillis[tiab]
"tendo achilli"[tiab]
tendo-achilli[tiab]
tendoachilli[tiab]
"achilles heel"[tiab]
heel-tendon[tiab]

“calcaneal tendon”[tiab]
“calcanean tendon”[tiab]
“calcaneus tendon”[tiab]
“tendo calcaneus”[tiab]
achillodynia[tiab]
“triceps surae”[tiab]
“calf muscle”[tiab]
“calf muscles”[tiab]
“calf musculature”[tiab]
gastrocnemius[tiab]
soleus[tiab]
mid-portion[tiab]
midportion[tiab]
“main body”[tiab]
midsubstance[tiab]

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Intervention:

“exercise therapy”[Mesh]
“exercise therapy”[tiab]
“exercise therapies”[tiab]
exercise[Mesh]
exercise[tiab]
exercises[tiab]
“eccentric training”[tiab]
“eccentric overload”[tiab]
“eccentric exercise”[tiab]
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“concentric training”[tiab]
“concentric overload”[tiab]
“concentric exercise”[tiab]
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training[tiab]
“resistance training”[Mesh]
“resistance training”[tiab]
“strength training”[tiab]

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Study designs:

randomized controlled trial[pt]
controlled clinical trial[pt]
randomized[tiab]
placebo[tiab]
clinical trials as topic[Mesh:noexp]
randomly[tiab]
trial[ti]

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#6 animals[mh] NOT humans[mh]
#7 #5 NOT #6

(((#1) AND #2) AND #3) AND #7

CHAPTER 3

Alfredson versus Silbernagel exercise therapy in chronic midportion Achilles tendinopathy: study protocol for a randomised controlled trial

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ABSTRACT

Background: Midportion Achilles tendinopathy (AT) is a common overuse injury, usually requiring several months of rehabilitation. Exercise therapy of the ankle plantar flexors (i.e. tendon loading) is considered crucial during conservative rehabilitation. Alfredson's isolated eccentric and Silbernagel's combined concentric-eccentric exercise programmes have both shown beneficial results, but it is unknown whether any of these programmes is superior for use in clinical practice. Therefore, the primary objective of this study is to compare the effectiveness of both programmes on clinical symptoms. Secondary objectives are to compare the effectiveness of both programmes on quality of life and functional outcome measures, to investigate the prognostic value of baseline characteristics and to investigate differences in cost-effectiveness.

Methods / Design: Eighty-six recreational male athletes (21-65 years of age) with unilateral chronic midportion AT (i.e. ≥ 3 months) will be included in this multicenter assessor blinded randomised controlled trial. They will be randomly allocated to either a group performing the Alfredson isolated eccentric training programme (n = 43), or a group performing the Silbernagel combined concentric-eccentric programme (n = 43). In the Alfredson group, participants will perform eccentric heel-drops on their injured side, twice daily for 12 weeks, whereas in the Silbernagel group, participants perform various concentric-eccentric heel-raise exercises, once daily for 12 weeks. Primary outcome measure will be the Victorian Institute of Sport Assessment – Achilles (VISA-A) questionnaire. Secondary outcomes will be a visual analogue scale (VAS) for pain during daily activities and sports, duration of morning stiffness, global perceived effect, the 12-item Short Form Health Survey and the Euroqol instrument, and functional performance measured with the heel-raise test and the countermovement jump. Additionally, alongside the RCT, a cost-effectiveness analysis will be performed. Assessments will be performed at baseline and after 12, 26, and 52 weeks.

Discussion: This study is the first to directly compare the Alfredson and the Silbernagel exercise programme in a randomised trial. The results can further enlarge the evidence base for choosing the most appropriate exercise programme for patients with midportion AT.

BACKGROUND

Midportion Achilles tendinopathy (AT) is a common overuse injury of the lower extremity,[1 2] most prevalent in male athletes who participate in sports that involve running and/or jumping.[2-4] When not adequately managed, the injury may cause long term absenteeism of sports and daily activities.[5] Treatment of midportion AT is initially conservative, usually requiring several months, with a plethora of possible treatment options.[6 7]

Historically, AT is considered as an inflammatory condition, but more recently it has been regarded as a failed healing response of the tendon, with minimal inflammatory influence.[8 9] In 2009, Cook and Purdam proposed a model that considers tendinopathy as a continuum, in which three somewhat interchangeable stages can be distinguished: 1) reactive tendinopathy, 2) tendon dysrepair, and 3) degenerative tendinopathy.[10] According to the authors, these stages all require tailored load management and exercise intervention strategies. The model was recently revisited,[11] but it is still generally agreed that exercise therapy (i.e. tendon loading) is crucial to promote improvement of symptoms and function.[3 9 12]

Several exercise programmes have shown favourable results in mid-portion AT, with both beneficial effects on pain and function. Recent studies concluded that there is strong evidence for eccentric exercise therapy,[6 7] particularly according to the Alfredson eccentric exercise programme.[13] In the Alfredson programme, the plantar flexor muscle-tendon unit is loaded eccentrically by performing heel drops on the injured side, while using the non-injured limb to (concentrically) return to the start position.[14] A total of 180 repetitions is performed daily, and this may be a great time-consuming burden for the patient, potentially compromising compliance and consequently the effectiveness of the programme. Although the majority of studies using the Alfredson programme reported significant improvements post-intervention,[14-17] it should be noted that other studies reported less positive effects.[18 19] Moreover, a recent study of Stevens & Tan (2014) showed that a less stringent "do-as-tolerated" eccentric protocol can lead to equal improvements in pain and function compared to the Alfredson protocol,[20] which may be advantageous from a patient perspective. However, as exercises were performed only for a period of six weeks, and mid- and long-term follow-up measurements (i.e. > six weeks) were lacking, conclusions should be interpreted with caution.

Also, exercise programmes other than isolated eccentric loading showed to be effective in AT.[21 22] In a recent randomised controlled trial (RCT), Beyer et al.[23] found that heavy slow resistance training (HSRT) using gym equipment leads to equally good clinical improvement compared with the Alfredson programme. Furthermore, in an earlier systematic review, Malliaras et al.[24] already concluded that there is equivalent evidence for the Silbernagel concentric-eccentric exercise programme, although this conclusion was based on limited evidence. Unlike the Alfredson protocol, the Silbernagel protocol also comprises concentric and even plyometric loading of the Achilles tendon.[25 26] From a patient perspective, a

potential benefit of the Silbernagel programme over the Alfredson programme, may be the frequency of the exercises (i.e. only once a day). This may encourage training compliance and consequently can result in better outcomes. Furthermore, a combination of concentric and eccentric loading may better restore concentric muscular deficits, as training gains are known to be specific to the contraction mode.[27]

Although both the Alfredson and Silbernagel programme have shown favorable results in midportion AT,[14 16 17 25 26 28 29] comparison of the results is hampered by heterogeneity of study populations.[13 24] Insight into whether one of these programmes is superior may lead to better results in the management of patients with AT.
This article provides a detailed description of the study design, target population, and methods/procedures of a pragmatic multicenter RCT that will investigate differences in effectiveness between the Alfredson and Silbernagel exercise programme for patients with midportion AT.

Study objectives
The primary objective of this study is to compare the effectiveness in terms of symptom reduction and function of the Alfredson isolated eccentric exercise programme to the Silbernagel concentric-eccentric exercise programme after 12 months in patients with chronic midportion AT.
Secondary objectives are 1) to investigate differences in effectiveness on global perceived effect and quality of life (QOL), 2) to investigate differences in effectiveness on functional outcome measures, and 3) to investigate the prognostic value of baseline characteristics. Furthermore, alongside this RCT, a cost-effectiveness evaluation between both programmes will be performed.

METHODS/DESIGN

Study design and setting
This protocol was developed in accordance with the SPIRIT guidelines,[30] and describes an assessor blinded multicenter parallel-group RCT, with a one-year follow-up. The study will be conducted in two different centers, that is the University Medical Center Utrecht (UMCU, department of Rehabilitation, Physical Therapy Science & Sports), Utrecht, The Netherlands, and Papendal Sports Medical Center, Arnhem, The Netherlands. Participants will be randomised to a group performing either the Alfredson isolated eccentric or the Silbernagel combined concentric-eccentric exercise programme. Randomisation will be performed using a web-based randomisation system, and allocation will be concealed. The investigators who are involved in baseline and follow-up measurements, and data analysis will be blinded to group allocation.

Measurements will be performed at baseline, and after 12, 26, and 52 weeks follow-up (see Figure 3.1). The study protocol is in accordance with Declaration of Helsinki, and has been approved by the ethics committee of the UMCU (registration number 16-158). The protocol was registered with the Dutch Trial Register on 7 January 2016 (NTR5638). Written informed consent will be obtained from all participants prior to their participation.

Participant selection
Recreational athletic patients (both male and female) with a clinical diagnosis of unilateral midportion AT, characterized by activity-related Achilles tendon pain and swelling at 2 to 7 cm from the calcaneal insertion,[31] are eligible for inclusion if they meet the following inclusion criteria: 1) 18-65 years of age, 2) duration of symptoms of at least 3 months, 3) participating in sports involving Achilles tendon loading (i.e. sports characterized by walking, running and/or jumping), and 4) able to comply with both exercise programmes.

Participants are excluded in case of: 1) bilateral symptoms, 2) diagnosis of insertional AT, 3) washout period of <4 weeks from other treatments for their AT, 4) corticosteroid injections in the region of the Achilles tendon in the previous 12 months, 5) other lower limb injuries of the affected limb in the previous 12 months, 6) musculoskeletal surgery of the affected limb in the previous 12 months, 7) history of Achilles tendon rupture in the affected limb, or 8) systemic diseases, such as rheumatoid arthritis or diabetes mellitus.

Sample size calculation
Sample size was calculated based on two high quality RCTs having investigated the Alfredson programme and the Silbernagel programme respectively, and using the VISA-A questionnaire as their primary outcome measure.[16 26] We used the respective change (mean ± standard deviation [SD]) in VISA-A scores for the groups that followed the above-mentioned exercise programmes:

- Rompe et al.[16] (n = 25): VISA-A Δ 22.4±19 for the Alfredson programme
- Silbernagel et al.[26] (n = 19): VISA-A Δ 34±17 for the Silbernagel programme

This resulted in an expected effect size of 0.64 between both exercise programmes, with an expected VISA-A change score that exceeds the minimal clinically important difference of 10 points.[23] Using G*Power 3.1, and assuming α two-sided = 0.05 and a power of 0.80, a total of 39 participants in each study arm was required. The dropout rate in the above-mentioned studies was 4%[26] and 9%[16] respectively. We chose to take the most conservative dropout rate of 9% into account, resulting in a required amount of 86 in total, that is 43 participants in each arm.

Recruitment and informed consent

Primarily, participants are recruited from the patient population of the two afore mentioned centers. Secondary, general practitioners and orthopedic surgeons in the surroundings of Papendal Sports Medical Center (Arnhem, The Netherlands), will be asked to identify participants.

Eligible participants will be informed about the study by their treating (sports) physician or physiotherapist through an information letter, and they will initiate contact with the coordinating investigator (BH). Eligibility criteria of these participants will initially be checked by telephone, and subsequently, if they meet the criteria, an appointment is made for baseline assessment. Prior to baseline assessment, eligibility criteria will be confirmed, and participants will sign informed consent.

Randomisation procedure

Randomisation will be performed directly after baseline assessment, by an independent secretary using a computer-generated random sequence table. Eighty-six envelopes will be prepared with a description of the allocated intervention (i.e., Alfredson or Silbernagel programme). These envelopes will be sealed, and then shuffled and sequentially numbered. After baseline assessment, the secretary will pick an opaque sealed envelope according to the randomisation table. Subsequently, within 1 week participants will be referred to one of the supervising physiotherapists, who is informed about the allocated programme by the independent secretary. During the first session, participants will receive detailed instructions on the allocated exercise programme.

The randomisation code will not be broken until the final follow-up measurement has been performed (i.e. participant's last visit), and data analysis has been completed. Participants are instructed not to reveal their group allocation to the investigator during all measurement procedures.

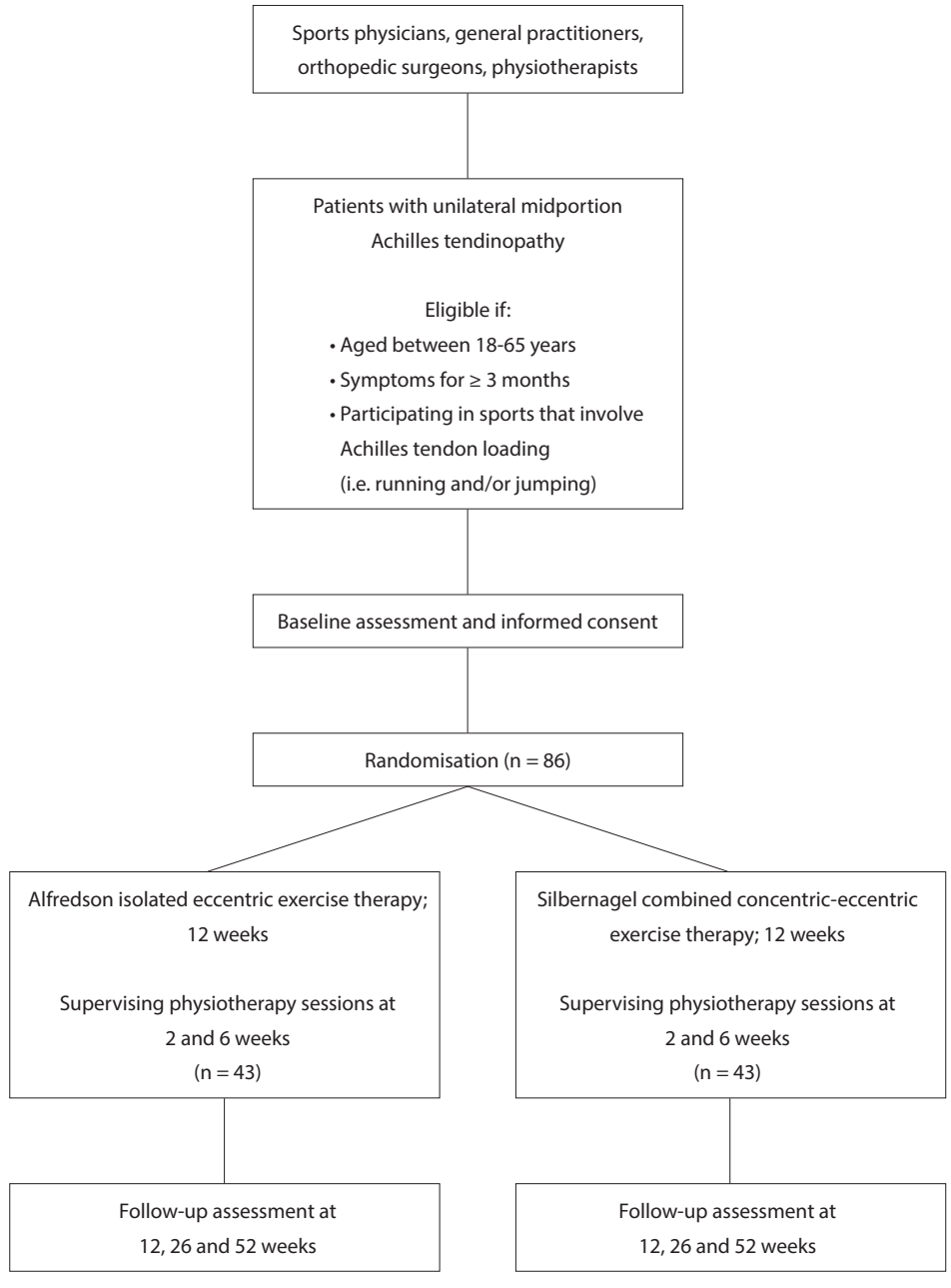

Figure 3.1 Flow chart of the study design

Intervention

One study arm performs the Alfredson isolated eccentric exercise programme,[14] which comprises 12 weeks of eccentric heel-drops on the injured limb, with the use of the uninjured limb to concentrically return to the start position. Exercises are performed twice daily, for three sets of 15 repetitions, both with a straight and bent knee (i.e. 180 repetitions each day). Non-disabling pain during the exercises is permitted, and load is added gradually in a backpack (in steps of 5 kg) when exercises can be performed without pain.

The second study arm performs an exercise programme according to the Silbernagel protocol.[25 26] This programme comprises various concentric and eccentric heel raise exercises, which are performed both on two legs and one leg, with three sets of 15 repetitions. The duration of the programme is also 12 weeks, and non-disabling pain during the exercises is also permitted, but contrary to the Alfredson programme, exercises are performed only once daily. Progression is made by changing from bipedal to unipedal exercises, by progressing from concentric-eccentric to purely eccentric loading, by adding weight in a backpack (in steps of 5 kg when pain did not exceed 5 on a 0-10 numerical rating scale), and finally by using fast-rebounding and plyometric exercises.

Table 3.1 depicts the key features of both exercise programmes. The timing of the exercise as well as the time under tension are not described, as we wanted to replicate the clinical prescription of the exercise programmes.

The content of both programmes will be instructed in detail by the supervising physiotherapists during the first appointment. Participants will perform all exercises from both programmes at home. After 2 and 6 weeks of training, an appointment with the supervising physiotherapist is made to discuss potential difficulties with the exercises and adjust load when possible.

During the intervention period, participants are asked to refrain from other treatments and from anti-inflammatory medication related to their injury. If they receive other (medical) treatments after the intervention period, they are asked to register this in a logbook.

Participants in both study arms are advised not to participate in any tendon loading sports activities (i.e. walking, running and jumping) during the first 3 weeks of the intervention period.[23] Subsequently, they are allowed to resume tendon loading sports activities, as long as pain does not exceed 50 mm on a 0-100 mm visual analogue scale (VAS), and pain subsides within 24 h after the activity.[26]

Table 3.1 Key features of the exercise programmes

	Alfredson	Silbernagel
Duration of exercise programme	12 weeks	12 weeks
Frequency of exercises	Twice daily	Once daily
Amount of exercises	2	4-5
Sets and repetitions	3x15	3x15
Exercise mode	Slow isolated eccentric	Concentric, eccentric, plyometric
Pain tolerated	Non-disabling pain	Not more than 5 on a 0-10 NRS
Progress	No pain	Phase 1-2-3
Progression	Add load (5 kg)	Add load (5 kg)

NRS = numerical rating scale

Education and monitoring

The research team will organize an information meeting in order to inform the involved physiotherapists of the two participating centers about the study procedures, their exact role, and the content of the exercise programmes. During this meeting, written information is also provided. For potential referrers, an information letter will be sent by the coordinating investigator. In this letter, the objectives of the study and a short description of the study design are described.

Monitoring of study procedures will be performed by an independent monitor during multiple visitations. These include an inspection of the study file for each center prior to the start of the study, and a check of the procedures and study files after 1 year and at the end of the study.

Outcome measures

Baseline assessment

During baseline assessment – besides the primary, secondary and other outcome measures – demographic and anthropometric characteristics such as age, weight, height, body mass index, job type and activity level, sport type and activity level, and referral type are recorded using a standardized questionnaire. Additionally, waist circumference will be recorded with a flexible tape measure,[32] range of motion for ankle dorsiflexion will be recorded using the weight bearing lunge test,[33] and dorsiflexion range of motion of the first metatarsophalangeal joint will be measured with a standard goniometer.[34] Body weight and sport activity level will also be recorded at T1, T2 and T3, as these variables are thought to vary throughout the study period and thus may potentially influence the study outcome.

Primary outcome measure
The primary outcome for this study will be the difference in VISA-A scores between both programmes after 12 months. The VISA-A questionnaire has been shown reliable and valid for evaluating clinical severity of symptoms of AT,[35] and was recently translated/validated in Dutch.[36] It consists of eight questions, covering the three domains of pain, and function in daily living and sporting activities. Scores range from 0 to 100, where 100 represents a perfect function.

Secondary outcome measures
A VAS will be used to evaluate severity of pain during sports and daily activities for the past 7 days. The VAS is a 100 mm horizontal line with two anchors, where zero represents 'no pain at all', and 100 represents 'the most severe pain'. It has been shown to be a valid and reliable method for evaluating pain levels.[37]

To determine whether participants feel that they have benefited from the intervention, global perceived effect (GPE) will be measured with the GPE scale.[38] This is a 7-point ordinal scale, ranging from "completely recovered" to "worse than ever".

The effect of the exercise programmes on QOL will be assessed with the 12-item Short Form Health Survey (SF-12)[39] and the Euroqol instrument (EQ-5D)[40] during baseline and follow-up measurements.

To assess functional performance of the muscle-tendon unit, two different tests with acceptable reliability (intraclass correlation coefficients 0.78-0.91) will be used. Firstly, participants will perform the heel-raise test,[41] which is recommended for the evaluation of calf muscle endurance in patients with AT.[42] Participants are asked to stand on one leg with a straight knee, supporting with their fingertips to the wall for balance. They are asked to perform as many heel raises as possible, with a straight knee and a frequency of one heel raise every 2 sec, avoiding forward body sway. The test is terminated when the participant stops, cannot keep the frequency, or when the technique is incorrect for two consecutive repetitions. The total number of heel raises will be used for data analysis. Secondly, the one-legged countermovement jump (CMJ) will be used to evaluate jump height.[42] This test has previously been used as a functional outcome measure in patients with midportion AT.[25] Although jump height is determined by many other muscle groups, research has shown that the calf muscle complex accounts for an important part of the CMJ movement.[43]

The CMJ is performed with the participant in an upright position on a jumping platform (Projump, Biometrics, The Netherlands), with the hands placed behind the back. Participants are asked to quickly bend their knee as much as they want and then immediately jump upwards to their maximum height. They are allowed three maximal trials, and the best jump height (in cm) is used for data analysis. Pain during the heel raise tests and CMJ is recorded on a 0-10 numerical pain rating scale.

Differences in cost-effectiveness between both programmes will be investigated by collecting several variables that are related to direct and indirect (medical) costs during follow-up assessments. These costs include medical consumption (visits to healthcare providers, supplementary diagnostics such as imaging, additional therapies such as insoles, braces, and medication use), and injury related absenteeism from (un)paid work, school, and sport.

Other outcome measures
Morning stiffness is common in patients with AT, and is considered a good indicator of tendon recovery.[3] Participants will rate their morning stiffness (in minutes) in a logbook. This logbook is also used to record compliance to the exercise programme. Compliance will be calculated by dividing the amount of exercises actually performed by the prescribed amount of exercises (i.e., 2x per day for the Alfredson group and 1x/day for the Silbernagel group). Subsequently, compliance will be categorized into four categories: poor (< 25%), moderate (between 25-50%), good (between 50-75%) and excellent (> 75%).[28]
Furthermore, participants will record other (medical) treatments and medication use in the logbook.

At baseline and follow-up measurements, the isometric strength of the hip extensors, abductors, and external rotators will be measured using a handheld dynamometer, according to previously reported methods.[44] Male patients with AT demonstrate diminished strength of their hip musculature compared to asymptomatic controls,[44] and by evaluating hip muscle strength over the course of this study, we try to investigate whether this is a prognostic factor in patients with AT.

Measurements
All measurements will be conducted at baseline (T0), at 12 weeks (i.e. termination of intervention, T1), 26 weeks (T2), and at 52 weeks (T3) follow up, and include both the afore mentioned questionnaires and physical examination. Participants can complete the questionnaires online (secured environment), by using a hyperlink that will be sent to them by e-mail. All physical assessments are conducted by the same investigator (BH), who is blinded to group allocation. For a detailed overview of all outcome measures collected in the course of the study and the respective follow-up times, see Table 3.2.

Statistical analyses
Differences between the Alfredson and Silbernagel group will be analyzed according to intention-to-treat (ITT) principle. If necessary, missing data will be imputed using multiple imputation. Descriptive statistics will be calculated for all continuous variables, and means and SDs will be reported (or median and interquartile range for non-parametric data). For nominal and categorical data, proportions will be calculated and reported.

Table 3.2 Overview of outcome measures collected in the course of the study

	Baseline	12 weeks	26 weeks	52 weeks
Eligibility criteria check	X			
Body height	X			
Body weight	X	X	X	X
BMI	X			
Job type & activity level	X			
Sport type & activity level	X	X	X	X
Referral type	X			
Waist circumference	X			
Dorsiflexion ROM ankle	X			
Dorsiflexion ROM first MTPJ	X			
VISA-A score	X	X	X	X
VAS for pain during sport and daily activities	X	X	X	X
Morning stiffness	X	X	X	X
Global perceived effect (7-point scale)	X	X	X	X
Quality of life (SF-12 and EQ-5D)	X	X	X	X
Functional performance (CMJ and heel raise test)	X	X		X
Variables related to cost-effectiveness:	X	X	X	X
- Medical consumption				
- Absenteeism from (un)paid work				
- Absenteeism from school				
- Absenteeism from sports activities				
Compliance to exercise programme		X		
Isometric strength of hip musculature	X	X		X

BMI = body mass index; *ROM* = range of motion; *MTPJ* = metatarsophalangeal joint; *VISA-A* = Victorian Institute of Sports Assessment – Achilles; *VAS* = visual analog scale; *SF 12* = 12-item short from health survey; *EQ-5D* = Euroqol instrument; *CMJ* = countermovement jump

Baseline comparability of the two groups will be assessed by the Student t-test (parametric data), and non-parametric tests where appropriate. To assess differences in (pseudo) metric data within and between the groups over time, an analysis of variance (ANOVA) will be performed, with post-hoc tests to correct for multiple testing. Multivariate regression techniques will be conducted to model the prognostic value of baseline variables on outcome. The cost-effectiveness will be estimated by calculating the incremental cost-effectiveness ratio: (costs of Silbernagel programme – costs of Alfredson programme) / (health benefit of Silbernagel programme – health benefit of Alfredson programme), and will be expressed as costs per quality adjusted life year (QALY).
All analyses will be performed with statistical significance level set at $\alpha = 0.05$ (two-sided).

DISCUSSION

Several studies showed that both Alfredson isolated eccentric and Silbernagel combined concentric-eccentric training are beneficial in terms of symptom reduction in midportion AT.[14 16 17 25 26] However, whether any of these programmes is more effective has yet to be determined. This study protocol describes the first RCT directly comparing the effectiveness of both programmes. We designed a pragmatic study, in which we try to replicate how both programmes are described in the clinical setting. By using the VISA-A – a condition-specific validated questionnaire that is widely recommended for use in research and clinical practice – as the primary outcome measure, we hope that comparison of our results to other studies and clinical practice will be enabled.

Besides the effectiveness on symptom reduction and QOL, our study also compares the effectiveness of both programmes on functional performance of the muscle-tendon unit. This comparison has not previously been performed, whilst research has shown that functional deficits of the muscle-tendon unit may still persist after one year in patients with AT, even though symptoms have fully recovered.[45]
We will also assess differences in cost-effectiveness in the mid-term and long term. Cost-effectiveness may be an important parameter for clinical decision making, but to date, research investigating cost-effectiveness in AT treatment is scarce.[17] We expect no difference in direct intervention-related costs, since both programmes are performed at home and the amount of supervising physiotherapy sessions is similar, but we are predominantly interested in potential differences in indirect costs (e.g. absenteeism of work, school and sports) between both programmes.

Recruitment for this trial will be performed in different institutions, that is sports medicine clinics, hospitals, and general practices. Therefore, participant characteristics may differ, and this potentially could lead to different subgroups of participants. No stratified randomisation for referral type is performed, but by including recreational athletes, it is expected that both study arms will consist of relatively homogeneous groups. Furthermore, we try to collect important participant characteristics that may cause potential bias to the results of this study. Nonetheless, it should be acknowledged that the participants' metabolic health is not fully covered, whilst research showed that this may be a confounding factor.[46]

We feel that the pragmatic nature of our study is a strength, as it mimics the clinical setting. Nevertheless, a potential limitation of this pragmatic design that we cannot draw any conclusions on the underlying mechanism of possible differences in effectiveness, since we have not controlled for many of the potential contributing factors.

Additionally, our study does not include a study arm performing no exercise intervention. Therefore, it remains unknown whether potential improvements are caused by the exercise programmes or by the natural course of the condition. Although it is generally agreed that exercise therapy is crucial in the treatment of AT,[3 9 12] we acknowledge that the lack of a non-exercise (wait-and-see) group is a potential limitation of the study design.

In summary, this multicenter two-arm RCT will compare the effectiveness of the Alfredson isolated eccentric to the Silbernagel combined concentric-eccentric programme for treatment of chronic midportion AT. The results of this study will enlarge the evidence base on different exercise programmes for AT, and may aid the clinician in choosing the most appropriate programme for their patients.

REFERENCES

1. Alfredson H. Chronic midportion Achilles tendinopathy: an update on research and treatment. *Clin Sports Med* 2003;22(4):727-41.
2. Zafar M, Mahmood A, Maffulli N. Basic science and clinical aspects of achilles tendinopathy. *Sports Med Arthrosc Rev* 2009;17(3):190-97.
3. Cook JL, Khan KM, Purdam C. Achilles tendinopathy. *Man Ther* 2002;7(3):121-30.
4. Sayana M, Maffulli N. Eccentric calf muscle training in non-athletic patients with Achilles tendinopathy. *J Sci Med Sport* 2007;10(1):52-58.
5. Cook J, Purdam CR. The challenge of managing tendinopathy in competing athletes. *Br J Sports Med* 2014;48(7):506-09.
6. Sussmilch Leitch SP, Collins NJ, Bialocerkowski AE, et al. Physical therapies for Achilles tendinopathy: systematic review and meta-analysis. *J Foot Ankle Res* 2012;5(1):15.
7. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.
8. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. *Arthroscopy* 1998;14(8):840-43.
9. Rees J, Maffulli N, Cook J. Management of tendinopathy. *Am J Sports Med* 2009;37(9):1855-67.
10. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. *Br J Sports Med* 2009;43(6):409-16.
11. Cook JL, Rio E, Purdam CR, et al. Revisiting the continuum model of tendon pathology: what is its merit in clinical practice and research? *Br J Sports Med* 2016;50(19):1187-91.
12. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: new treatment options. *Br J Sports Med* 2007;41(4):211-16.
13. Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: A systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.
14. Alfredson H, Pietilä T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26(3):360-66.
15. Fahlström M, Jonsson P, Lorentzon R, et al. Chronic Achilles tendon pain treated with eccentric calf-muscle training. *Knee Surg Sports Traumatol Arthrosc* 2003;11(5):327-33.
16. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2009;37(3):463-70.
17. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med* 2011;45(5):421-28.
18. Maffulli N, Walley G, Sayana MK, et al. Eccentric calf muscle training in athletic patients with Achilles tendinopathy. *Disabil Rehabi*l 2008;30(20-22):1677-84.
19. Ram R, Meeuwisse W, Patel C, et al. The limited effectiveness of a home-based eccentric training for treatment of Achilles tendinopathy. *Clin Invest Med* 2013;36(4):E197-206.
20. Stevens M, Tan CW. Effectiveness of the Alfredson protocol compared with a lower repetition-volume protocol for midportion Achilles tendinopathy: a randomized controlled trial. *J Orthop Sports Phys Ther* 2014;44(2):59-67.
21. Kjaer M, Heinemeier KM. Eccentric exercise: acute and chronic effects on healthy and diseased tendons. *J Appl Physiol* (1985) 2014;116(11):1435-38.
22. Bohm S, Mersmann F, Arampatzis A. Human tendon adaptation in response to mechanical loading: a systematic review and meta-analysis of exercise intervention studies on healthy adults. *Sports Med Open* 2015;1(1):7.
23. Beyer R, Kongsgaard M, Hougs Kjaer B, et al. Heavy slow resistance versus eccentric training as treatment for Achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2015;43(7):1704-11.
24. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.
25. Silbernagel KG, Thomee R, Thomee P, et al. Eccentric overload training for patients with chronic Achilles tendon pain--a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports* 2001;11(4):197-206.
26. Silbernagel KG, Thomeé R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35(6):897-906.
27. Morrissey MC, Harman EA, Johnson MJ. Resistance training modes: specificity and effectiveness. *Med Sci Sports Exerc* 1995;27(5):648-60.
28. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41(7):e1-e6.
29. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9(1):42-47.
30. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;58(3):200-07.
31. van Dijk CN, van Sterkenburg MN, Wiegerinck JI, et al. Terminology for Achilles tendon related disorders. *Knee Surg Sports Traumatol Arthrosc* 2011;19(5):835-41.
32. Gaida JE, Alfredson H, Kiss ZS, et al. Asymptomatic Achilles tendon pathology is associated with a central fat distribution in men and a peripheral fat distribution in women: a cross sectional study of 298 individuals. *BMC Musculoskelet Disord* 2010;11:41.
33. Konor MM, Morton S, Eckerson JM, et al. Reliability of three measures of ankle dorsiflexion range of motion. *Int J Sports Phys Ther* 2012;7(3):279-87.

34. Allen RH, Gross MT. Toe flexors strength and passive extension range of motion of the first metatarsophalangeal joint in individuals with plantar fasciitis. *J Orthop Sports Phys Ther* 2003;33(8):468-78.

35. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

36. Van Sterkenburg MN. Achilles tendinopathy: new insights in cause of pain, diagnosis and management. University of Amsterdam, 2012.

37. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 2005;14(7):798-804.

38. Kamper SJ, Ostelo RW, Knol DL, et al. Global Perceived Effect scales provided reliable assessments of health transition in people with musculoskeletal disorders, but ratings are strongly influenced by current status. *J Clin Epidemiol* 2010;63(7):760-66.e01.

39. Mols F, Pelle AJ, Kupper N. Normative data of the SF-12 health survey with validation using postmyocardial infarction patients in the Dutch population. *Qual Life Res* 2009;18(4):403-14.

40. Hurst NP, Kind P, Ruta D, et al. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Br J Rheumatol* 1997;36(5):551-59.

41. Moller M, Lind K, Styf J, et al. The reliability of isokinetic testing of the ankle joint and a heel-raise test for endurance. *Knee Surg Sports Traumatol Arthrosc* 2005;13(1):60-71.

42. Silbernagel KG, Gustavsson A, Thomeé R, et al. Evaluation of lower leg function in patients with Achilles tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2006;14(11):1207-17.

43. Mackala K, Stodolka J, Siemienski A, et al. Biomechanical analysis of squat jump and countermovement jump from varying starting positions. *J Strength Cond Res* 2013;27(10):2650-61.

44. Habets B, Smits HW, Backx FJG, et al. Hip muscle strength is decreased in middle-aged recreational male athletes with midportion Achilles tendinopathy: a cross-sectional study. *Phys Ther Sport* 2016;25:55-61.

45. Silbernagel KG, Thomeé R, Eriksson BI, et al. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med* 2007;41(4):276-80.

46. Ackermann PW, Hart DA. General overview and summary of concepts regarding tendon disease topics addressed related to metabolic disorders. *Adv Experiment Med Biol* 2016;920:293-98.

CHAPTER 4

No difference in clinical effects when comparing Alfredson eccentric and Silbernagel combined concentric-eccentric loading in Achilles tendinopathy: a randomised controlled trial

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ABSTRACT

Background: Alfredson isolated eccentric and Silbernagel concentric-eccentric loading both showed beneficial effects on clinical symptoms in midportion Achilles tendinopathy (AT), but were never directly compared to each other.

Purpose: To test for differences in clinical effects at one-year follow-up between Alfredson and Silbernagel loading in midportion AT.

Study design: Single-blind randomised controlled trial.

Methods: Forty recreational athletes were allocated to the Alfredson group (AG) or the Silbernagel group (SG). Primary outcome was the difference in the Victorian Institute of Sports Assessment – Achilles (VISA-A) at one-year follow-up. Secondary, the visual analog scale for pain during daily (VAS-ADL) and sports activities (VAS-sports), the Euroqol instrument (EQ-5D), and global perceived effect (GPE) were assessed. Measurements were performed at baseline, and 12-week, 26-week, and one-year follow-up. Analysis was performed using a linear mixed regression model with intervention (AG versus SG), time (i.e. 12, 26 and one year) and intervention-by-time interaction.

Results: The VISA-A score improved from 60.7±17.1 at baseline to 89.4±13.0 at one-year follow-up ($P < 0.001$) and from 59.8±22.2 to 83.2±22.4 ($P < 0.001$) in the AG and SG respectively. As the interaction term did not significantly improve the model, we report a treatment effect without interaction term, indicating a constant difference at each follow-up. The linear mixed model with correction for baseline VISA-A and confounders, revealed a non-significant treatment effect (2.4, 95% CI [-8.5, 13.3], $P = 0.656$). Additionally, after adjustment for the respective baseline values and confounders, non-significant treatment effects were found for the VAS-ADL (-2.0, 95% CI [-11.3, 7.3], $P = 0.665$), and VAS-sport (1.3, 95% CI [-12.8, 15.3], $P = 0.858$). Subscales of the EQ-5D improved in both groups. After one year, significantly more participants in the SG considered themselves improved (GPE: AG: 50.0%, SG: 77.3%; $P = 0.04$).

Conclusion: No differences in clinical effects were found between Alfredson and Silbernagel loading up to one-year follow-up. Both programmes significantly improved clinical symptoms, and given the high adherence rates, offering either of them as home-based programme with limited supervision appears an effective treatment strategy for midportion AT.

INTRODUCTION

In recent decades, loading programmes have become the cornerstone of treatment for midportion Achilles tendinopathy (AT), mainly based on the work of Alfredson et al.[1] These authors showed that recreational runners who performed 12 weeks of eccentric heel-lowering exercises daily demonstrated significantly larger pain reduction compared to a group who did not exercise. Although these promising results were not always confirmed in later studies,[2 3] the effectiveness of the Alfredson programme for treating midportion AT in an active population is well-documented within the literature.[4 5]

Silbernagel et al. showed that a combination of multiple concentric and eccentric heel-raising exercises performed once daily for 12 weeks also effectively improved clinical symptoms in those with AT.[6 7] The Silbernagel programme involved uni and bipedal exercises, as well as progression to faster concentric-eccentric exercises and finally plyometrics. In a systematic review, Malliaras et al.[8] concluded that this Silbernagel programme, yields equivalent clinical results compared to the Alfredson eccentric programme. However, their conclusion was based on heterogeneous study populations, hampering a firm conclusion regarding superiority of any programme. To date, no studies have directly compared both loading programmes. Therefore, we aimed to test for differences in clinical effects between the Alfredson isolated eccentric and the Silbernagel combined loading programme in recreational athletes with midportion AT in a randomised controlled trial with one-year follow-up. In line with extant, yet inconclusive research,[8] we hypothesized that both programmes would yield comparable results.

METHODS

Study design

A prospective multicenter two-arm single blind randomised clinical trial (RCT) was conducted in agreement with the CONSORT statement.[9] Participants were allocated either to the Alfredson isolated eccentric programme (Alfredson group; AG) or the Silbernagel concentric-eccentric exercise programme (Silbernagel group; SG). Researchers involved in data collection and analysis were blinded to group allocation. Measurements were performed at baseline and after 12 weeks (T1), 26 weeks (T2), and one year (T3). The study protocol was prospectively registered in the Dutch trial register (NTR5638) and was approved by the research ethics committee of the University Medical Center Utrecht (16-158/M). Detailed information on the study design was published earlier.[10]

Participants

Recreational athletes with chronic (i.e. ≥ 3 months) unilateral midportion AT were eligible for inclusion if they were aged between 18-65 years and participated in sports that involved Achilles tendon loading. Exclusion criteria were 1) bilateral symptoms, 2) insertional

AT, 3) washout period of less than four weeks from other treatments,[11] 4) corticosteroid injections in the region of the Achilles tendon in the previous 12 months, 5) other lower limb injuries of the affected limb in the previous 12 months, 6) musculoskeletal surgery of the affected limb in the previous 12 months, 7) history of Achilles tendon rupture in the affected limb, and 8) systemic diseases that could interfere with the rehabilitation (e.g. rheumatoid arthritis or diabetes).

The diagnosis of midportion AT was established by one of the researchers (BHa), with over 12 years of experience in tendon rehabilitation. Diagnosis was based on the following criteria: subjective as well as palpation pain 2-7 cm proximal to the calcaneal insertion,[12] pain during tendon loading sports activities, swelling and morning stiffness.[13] No imaging modalities were used to assist in establishing the clinical diagnosis.[14]

An a priori sample size calculation was performed based on the differences on the Victorian Institute of Sports Assessment – Achilles (VISA-A) obtained in previous studies.[6 15] These studies found an average±standard deviation (SD) improvement of 22.4±19[15] and 34±17[6] points on the VISA-A for the Alfredson and the Silbernagel programme respectively. With 0.80 power and α (two-sided) = 0.05, and taking a drop-out rate of 9% into account, we needed a total of 86 participants to detect a difference of 11.6 points on the VISA-A.

Recruitment and randomisation

A detailed description of our recruitment strategy is given elsewhere.[10] Participants were primarily recruited through sports physicians and physiotherapists from Sports Medical Center Papendal and the University Medical Center Utrecht (both in the Netherlands). To enhance enrollment of participants, three Dutch private clinics for physiotherapy were added as participating centers (FysioHolland Medicort, Academie Instituut and Van Tongeren Fysiotherapie). After being informed, participants made an appointment with one of the researchers (BHa) to check for the diagnosis of midportion AT and the other criteria for inclusion in this study. Prior to participation, participants signed informed consent. Thereafter, baseline assessment was performed, and an independent secretary randomised the participants into the AG or the SG by choosing an opaque sealed envelope from a box. Envelopes were consecutively numbered according to a computer-generated randomisation table. Within one week after baseline assessment, participants were scheduled for an appointment with one of the supervising physiotherapists, who were informed about the allocated programme by the secretary. During this appointment, the respective programme was explained so that participants could correctly perform the exercises at home. Two and six weeks later, an appointment with the same supervising physiotherapist was scheduled, with the aim to motivate participants to continue their exercises and adjust the programme according to the protocol.

Interventions

In the AG, participants performed 12 weeks of home-based heavy load eccentric heel-lowering exercises on the edge of a stair, using the non-injured limb to concentrically return to the starting position.[1] Exercises were performed twice daily, for three sets of 15 repetitions with a straight knee, and three sets of 15 repetitions with a bent knee. Pain during exercises was allowed, and load was increased by adding weight in a backpack in steps of 5 kg, once exercises could be performed without pain.

The SG followed 12 weeks of home-based concentric-eccentric loading. Various heel-raising exercises were performed once daily, with three sets of 15 repetitions for each exercise. Progression was made from bipedal to unipedal exercises, from floor level to the edge of a stair, by increasing weight in 5 kg steps, and by increasing speed (plyometrics) in the last phase. More detailed description of the programmes are published elsewhere.[6]

Participants in both study arms were asked to refrain from other treatments during the intervention period, yet if they received other treatments, they were requested to register this in a logbook. Furthermore, they were asked to register exercise adherence in the logbook weekly. During the first three weeks of their programme, participants were advised not to engage in tendon-loading sports activities, such as running and jumping. After the first three weeks, they could resume their sports activities with a pain-monitoring model, that is pain during activities should not exceed 5 on a 0-10 numerical rating scale, and symptoms should have subsided within 24 h after the respective activity.[6] After the intervention, participants were encouraged to continue loading exercises according to their allocated programme, but this was not further monitored.

Outcome measures

The primary outcome measure was the valid and reliable Dutch version of the VISA-A,[16] which consists of eight questions, covering the domains of pain, daily activities and sport. Scores range from 0-100, with 100 being equivalent to asymptomatic.[17]

As secondary outcome measures, we included the visual analogue scale (VAS) for pain, on which participants could indicate their pain during daily activities (VAS-ADL) and sports activities (VAS-sports) during the previous week. VAS scores ranged from 0-100, with 100 representing maximal pain. Participants also completed the Euroqol instrument (EQ-5D) for quality of life[18], in which they rated five dimensions of health on a three-point scale (no problems, some problems, extreme problems) and a VAS for self-rated health. Lastly, participants rated their global perceived effect (GPE) on a 7-point ordinal scale, ranging from 'worse than ever' to 'completely recovered'.

Demographic data collected at baseline were age, sex, body height/weight, body mass index (BMI), and duration of symptoms. Additionally, we collected waist circumference with a flexible tape measure,[19] ankle dorsiflexion range of motion (ROM) of the talocrural joint using the weight bearing lunge test,[20] and dorsiflexion ROM of the first metatarsophalangeal joint using a goniometer (Fysiosupplies, Groningen, The Netherlands).[21] A detailed description of all measurement procedures was previously published.[10]

Statistical analyses

The statistical analysis was performed using SPSS 23.0, based on intention-to-treat principles. Testing was performed two-sided, with significance level set at $\alpha \leq 0.05$.

Patient characteristics were presented as means±SD or numbers (percentage). Statistical comparison of baseline characteristics between the groups was not performed in line with current recommendations.[22]

Adherence rate was defined as the proportion of prescribed exercises actually performed and was divided into four categories: when < 25%, 25-50%, 50-75%, or >75% of the exercises was performed, adherence was rated as "poor", "moderate", "good", or "excellent" respectively.[23] Between-group difference in adherence rate was analyzed using the Pearson's X^2-test.

Prior to further analysis, normality was examined, and a graphical representation of observed mean scores and 95% confidence intervals (CIs) was composed.

Our primary aim was to test for differences in VISA-A score between the AG and the SG at one-year follow-up. Secondary, we assessed differences in the VAS-ADL and VAS-sports at one-year follow-up. As our data showed some missing data in the follow-up measurements, we decided to use a linear mixed regression model for analysis of our primary and secondary outcomes instead of the repeated measures ANOVA we intended to apply.[10] We included an unstructured residual covariance type (GEE type) to correct for repeated measurements within participants. For the main analysis, we used a linear model that included intervention (AG versus SG), time (i.e. 12-week, 26-week and one-year follow-up) and intervention-by-time interaction. We evaluated the intervention-by-time interaction effect for all outcomes and tested these with likelihood ratio tests. In case the interaction did not significantly improve the model fit, an additional step was performed in which we excluded the interaction from the analysis to test an assumption of a constant difference between AG and SG at each follow-up. Validity of the model was assessed using residual analyses.[24]

Regression analyses were performed with the VISA-A, the VAS-ADL, and VAS-sports during follow-up as dependent variables. For each analysis, the baseline value of the respective outcome was included as covariate. Additionally, sex, age, and duration of symptoms were included as covariates, since these were considered potential confounders.[25 26]

For completeness, we report the results for the initial model (intervention, time and intervention-by-time interaction), the model with correction for baseline, and the model with correction for baseline and confounders. Results for each follow-up measurement are presented as treatment effects (mean [95% CI]) with the AG as reference, based on estimated marginal means. Additionally, as the intervention-by-time interaction term did not improve our model fit, we present a constant treatment effect (95% CI) with the AG as reference, corrected for baseline and confounders, but without the intervention-by-time interaction.

For the EQ-5D subscales, the percentage of participants reporting each level of each problem was calculated for all measurements, and for the EQ-5D VAS score we calculated mean±SD for all measurements.[27] Differences between the groups for the GPE were assessed using Pearson's X^2.

RESULTS

Due to a much slower than expected inclusion rate, and the outbreak of COVID-19, we decided to terminate enrollment of new participants in April 2020, prior to reaching the targeted sample size. Planned follow-up measurements after this date were performed as scheduled. From December 2016 to April 2020, a total of 107 potential participants were screened for eligibility (Figure 4.1). Of these, forty participants were included and randomised into the AG (n = 18) or the SG (n = 22). Two participants in the AG withdrew from the study, one due to lack of time and one for an unknown reason. In the SG, one participant decided to withdraw due to aggravation of symptoms after a running race. Data of these participants was included in the analyses.

Baseline characteristics of the study sample are presented in Table 4.1. Participants in the AG were younger (45 years) than the SG (50 years) and experienced a shorter duration of symptoms (9.4 months) than participants in the SG (15.1 months). Furthermore, the AG consisted of less runners (5.6%) than the SG (27.3%).

Table 4.1 Baseline characteristics of study population

	Alfredson group (n = 18)	**Silbernagel group (n = 22)**
Sex (female) N (%)[a]	8 (44.4%)	10 (47.6%)
Age (years)[a]	44.7±9.0	49.9±10.1
Height (cm)[a]	179.7±8.6	175.4±9.8
Weight (kg)[a]	84.7±15.6	81.3±15.4
BMI (kg/cm2)[a]	26.1±3.6	26.3±4.1
Injured limb (%)	12 left (66.7%)	11 left (50.0%)
Duration of symptoms (months)[a]	9.4±8.2	15.1±24.0
Sport type N (%)		
- Walking	8 (44.4%)	6 (27.3%)
- Running	1 (5.6%)	6 (27.3%)
- Ball sports	9 (50.0%)	7 (31.8%)
- Other sports	-	1 (4.5%)
- No current sport	-	2 (9.1%)
Weekly time spent on sport (h)[a]	4.7±4.7	5.1±3.5
Waist circumference (cm)[a]	94.3±11.5	94.8±12.6
ROM dorsiflexion TCJ (cm)[a]		
- Injured limb	12.4±3.0	10.5±2.6
- Non-injured limb	12.5±3.7	10.1±3.5
ROM dorsiflexion MTP1 (°)[a]		
- Injured limb	44.7±14.2	43.1±10.9
- Non-injured limb	46.2±13.8	43.6±11.2
VISA-A[a]	60.7±17.1	59.8±22.2
VAS-ADL[a]	28.6±22.1	28.6±31.8
VAS-sports[a]	44.8±26.8	46.6±32.6

BMI = body mass index; *ROM* = range of motion; *TCJ* = talocrural joint; *MTP1* = first metatarsophalangeal joint; *VISA-A* = Victorian Institute of Sports Assessment – Achilles; *VAS* = visual analog scale; *ADL* = activities of daily life
[a] data reported as mean±standard deviation

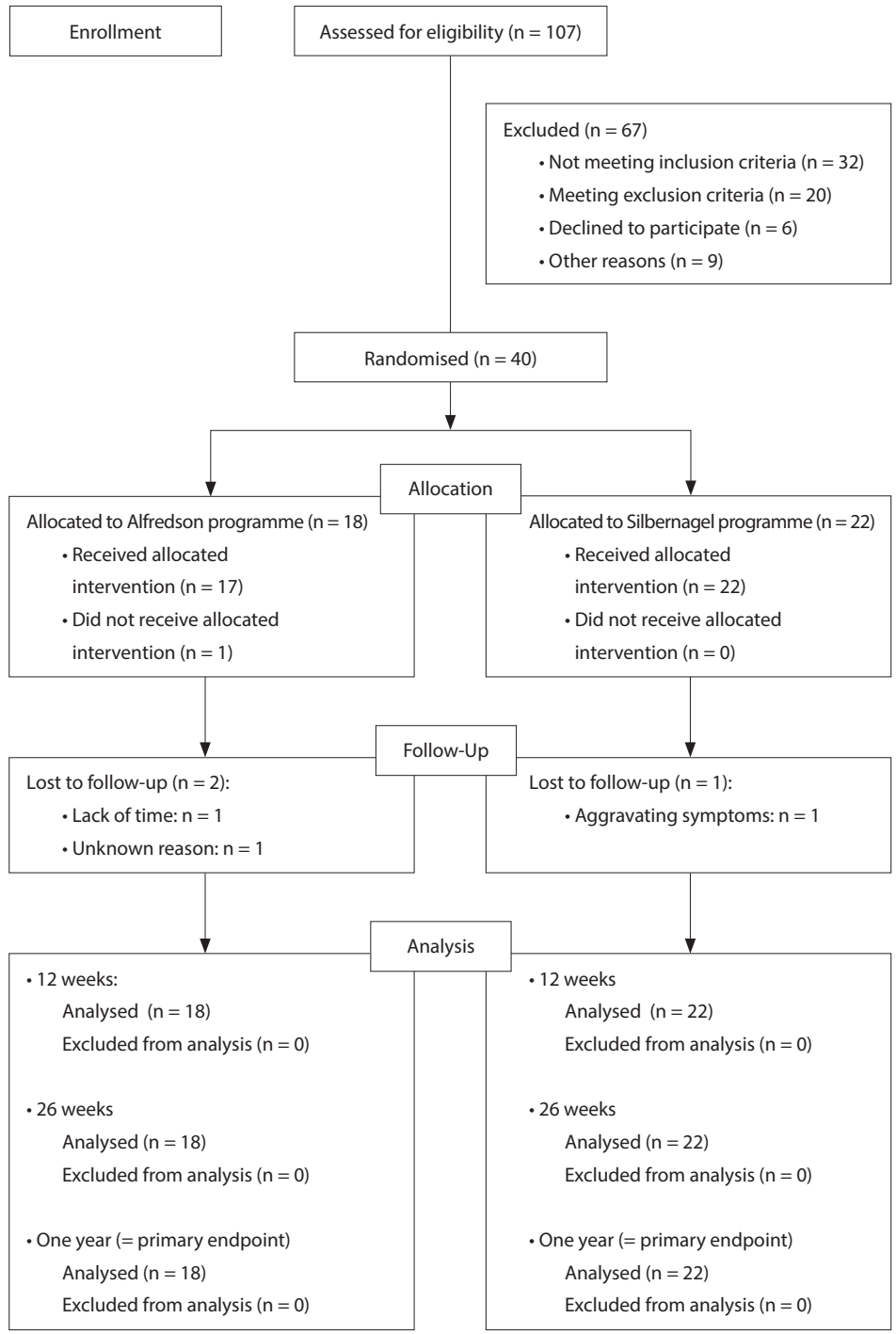
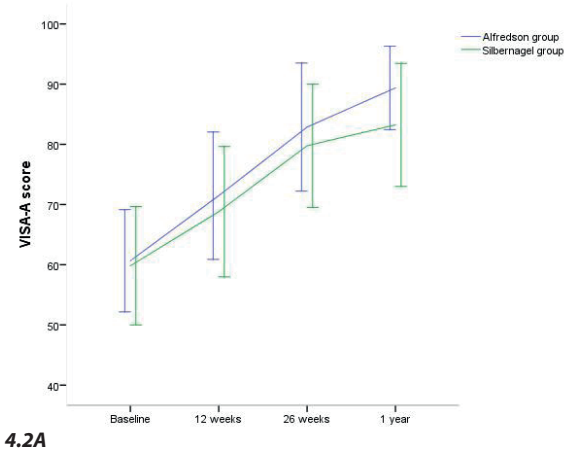


Figure 4.1 Flow chart of the study population throughout the study

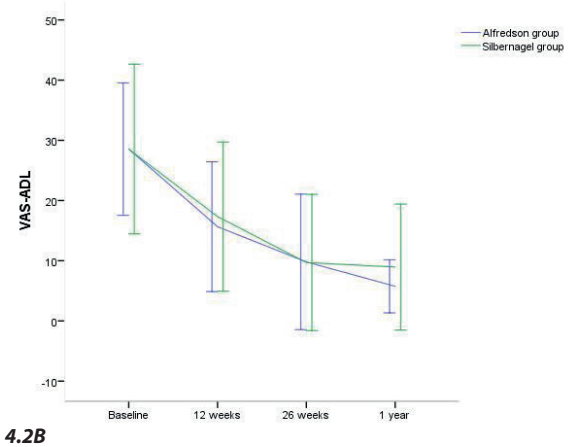
In the AG, one participant was treated once with dry needling and kinesiotape, two participants received inlays, and two participants used paracetamol for a period of one week. In the SG, one participant received massage of the calf musculature (once weekly for four weeks), one participant received heel lifts, one participant was treated once with shockwave therapy, and three participants used non-steroid anti-inflammatory medication or paracetamol for a short term.

Adherence

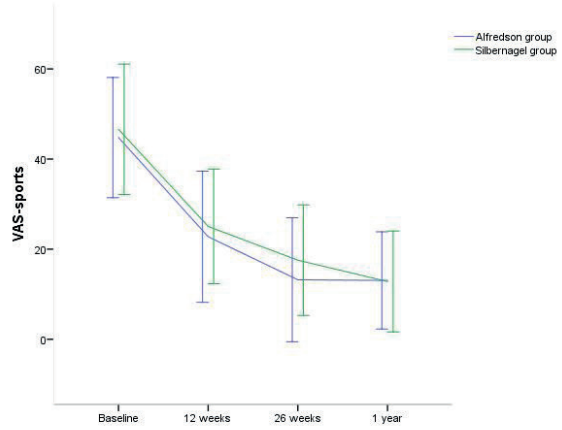
Mean adherence rate during the intervention period was 74.1±21.6% in the AG and 77.3±16.2% in the SG. In the AG, 20% showed "good" and 53% showed "excellent" adherence. For the SG, these percentages were 40% and 50% respectively. Analysis revealed no significant difference in adherence rates between both groups ($X^2 = 4.8$, $P = 0.197$).



4.2A



4.2B



4.2C

Figure 4.2 (A-C) Observed mean scores with 95% confidence intervals of the VISA-A (4.2A), VAS-ADL (4.2B) and VAS-sports (4.2C) from baseline to one-year follow-up.

Primary outcome measure

In the AG, the VISA-A score improved from 60.7±17.1 at baseline to 89.4±13.0 at one-year follow-up (Figure 4.2A; $P < 0.001$), whereas in the SG, the VISA-A score increased from 59.8±22.2 to 83.2±22.4 ($P < 0.001$). Table 4.2 reports the estimated marginal means for each follow-up measurement (i.e. 12 weeks, 26 weeks and one year), with correction for baseline and confounders and using the intervention-by-time interaction. As the interaction term did not improve the model fit, we report a treatment effect without the interaction term, indicating a constant difference at each follow-up up to one year. Linear mixed model analysis without the interaction term showed a non-significant treatment effect (2.4, 95% CI [-8.5, 13.3], $P = 0.656$, Table 4.3) for the AG after correcting for baseline VISA-A and confounders.

Secondary outcome measures

The VAS-ADL showed a decrease of 28.6±22.1 at baseline to 5.8±8.3 at one-year follow-up for the AG (Figure 4.2B; $P = 0.004$). In the SG, VAS-ADL decreased from 28.6±31.8 to 9.0±23.0 ($P = 0.004$). The estimated marginal means at the different follow-up measurements are given in Table 2. After correction for baseline VAS-ADL and confounders, the linear mixed model analysis without the group-by-time interaction revealed a constant non-significant treatment effect (-2.0, 95% CI [-11.3, 7.3], $P = 0.665$, Table 4.3).

In the AG, VAS-sport decreased from 44.8±26.8 at baseline to 13.1±20.2 at one-year follow-up (Figure 4.2C; $P = 0.027$), whereas in the SG, VAS-sport improved from 46.6±32.6 to 12.8±24.6 ($P = 0.027$). Without including the intervention-by-time interaction, a non-significant treatment effect (1.3, 95% CI [-12.8, 15.3], $P = 0.858$, Table 4.3) was found after adjustment for baseline VAS-sport and confounders.

Table 4.2 Comparison of primary and secondary outcomes in the Alfredson versus the Silbernagel group

	Without correction		With correction for baseline		With correction for baseline and confounders[a]	
	Treatment effect[b] (95% CI)	*P*-value	Treatment effect[b] (95% CI)	*P*-value	Treatment effect[b] (95% CI)	*P*-value
VISA-A score						
12 weeks	2.1 [-12.2, 16.4]	0.772	2.1 [-10.7, 14.8]	0.741	0.9 [-11.9, 13.8]	0.885
26 weeks	2.2 [-11.4, 15.8]	0.741	2.2 [-10.4, 14.8]	0.728	1.1 [-11.8, 14.0]	0.867
1 year	5.6 [-6.6, 17.9]	0.360	5.5 [-6.5, 17.5]	0.361	4.3 [-8.0, 16.6]	0.479
VAS-ADL						
12 weeks	-1.3 [-16.9, 14.3]	0.866	-1.6 [-13.2, 10.0]	0.784	-0.9 [-12.4, 10.6]	0.874
26 weeks	3.2 [-11.2, 17.7]	0.653	3.6 [-8.5, 15.6]	0.552	4.5 [-8.1, 17.0]	0.475
1 year	-1.3 [-13.2, 10.6]	0.825	-0.8 [-10.7, 9.1]	0.864	-0.1 [-10.3, 10.1]	0.986
VAS-sports						
12 weeks	-1.8 [-19.6, 16.1]	0.843	-1.6 [-19.0, 15.7]	0.849	-0.7 [-18.3, 16.9]	0.936
26 weeks	-1.9 [-18.5, 14.6]	0.816	-1.8 [-18.2, 14.6]	0.824	-1.0 [-17.6, 15.7]	0.908
1 year	2.0 [-12.9, 16.9]	0.789	2.0 [-12.8, 16.7]	0.788	2.9 [-12.3, 18.1]	0.702

CI = confidence interval; *VISA-A* = Victorian Institute of Sports Assessment – Achilles; *VAS* = visual analogue scale; *ADL* = activities of daily life
[a] Baseline measurement of respective outcome, sex, age, and duration of symptoms
[b] Treatment effects reported with the Alfredson group as reference

Table 4.3 Treatment effect between the Alfredson and Silbernagel group

	With correction for baseline and confounders[a]	
	Treatment effect[b] (95% CI)	*P*-value
VISA-A score	2.4 [-8.5, 13.3]	0.656
VAS-ADL	-2.0 [-11.3, 7.3]	0.665
VAS-sports	1.3 [-12.8, 15.3]	0.858

CI = confidence interval; *VISA-A* = Victorian Institute of Sports Assessment – Achilles; *VAS* = visual analogue scale; *ADL* = activities of daily life
[a] Baseline measurement of respective outcome, sex, age, and duration of symptoms
[b] Treatment effects reported with the Alfredson group as reference group

The results for the EQ-5D are given in Appendix 4.1. In both groups, the percentage of participants reporting 'no problems' on the domains mobility, usual activities and pain/discomfort increased between baseline and one year follow-up. In the SG, more than 25% of the participants encountered some problems with anxiety/depression at baseline, but this percentage decreased from 27.3% to 14.3% at one-year follow-up. In the AG, none of the participants reported any problems on anxiety/depression during the study. The EQ-5D VAS-score changed from 77.2±13.1 at baseline to 77.9±23.4 at one-year follow-up in the SG, and from 82.6±8.7 to 81.0±20.3 in the AG, indicating no improvement in self-rated health of the participants up to one-year follow-up.

The GPE showed that, at one-year follow-up, 50% of the participants in the AG reported "much" or "very much" improvement, whereas this percentage in the SG was 77.3%. This difference was statistically significant ($X^2 = 10.3$, $P = 0.04$).

DISCUSSION

In this RCT, we found that both the Alfredson and the Silbernagel programme yield significant improvement of clinical symptoms up to one-year follow-up in recreational athletes with midportion AT, but no significant differences between both programmes were found. QOL and perceived effect also improved in both groups, with significantly more participants in the SG who considered themselves improved at one-year follow-up in comparison with the AG.

Improvement on the VISA-A and the VAS-scores between baseline and one-year follow-up, which was found within both groups, exceeded the minimal clinically important difference (MCID) reported for these outcome measures.[28-30] These positive clinical results are frequently reported for both the Alfredson and the Silbernagel loading programme in patients with midportion AT,[4 8] with the VISA-A score considered the most relevant patient-reported outcome measure.[28] For the Silbernagel programme, an increase of 28-34 points in the VISA-A has been reported,[6] whilst increase of the VISA-A score for the Alfredson programme ranged between 18-25 points.[23 31 32] Baseline VISA-A values in the current study were comparable to those reported in other studies,[6 32] but at one-year follow-up our results were slightly different from data reported elsewhere. On the one hand, improvement of VISA-A score for the SG in the current study (23.7 points) was slightly inferior to the 28-34 points found elsewhere.[6] On the other hand, improvement for the AG obtained in the current study (i.e. increase of 29.3 points on the VISA-A) exceeded the results reported in other studies (18-25 points increase of the VISA-A).[23 31 32] The precision of the estimates found in the current study, may be affected by our small sample size, comparison of effect sizes with other studies is therefore complicated. However, we feel that some explanations may account for the discrepancies in effect sizes found in other studies. Primarily, although load progression in the current study was applied according to the

original protocols, we did not exactly monitor the amount of weight that each participant added during the course of the exercise programme. Therefore, there may be a discrepancy between the current study and other AT exercise trials in the amount of weight added. Secondly, the frequency of supervision in the current study (i.e. three times in 12 weeks) differed from the frequency of supervision in the original study using the Silbernagel programme (i.e. 12 times in 12 weeks)).[7] This may explain why higher VISA-A change scores were found in the original Silbernagel study,[6] compared with our results. Lastly, differences in follow-up term may account for differences in effect sizes. Rompe et al. assessed the Alfredson programme using a 16-week follow-up, which was different from the follow-up terms used in the current study. The change score in VISA-A reported at 16-week follow-up in their study was comparable to our findings at 26-week follow-up, but inferior to our results at one-year follow-up.[31]

Our data shows that clinical symptoms continue to improve in the long term, both for the AG and SG. This is in accordance with other research, showing improvement of the VISA-A score up to five years after following these programmes.[33 34] However, despite a continuous improvement over the course of the study, our results illustrate that many participants still encountered mild symptoms at one-year. In both groups, the mean VISA-A score at one year did not exceed 90 points, which is considered the lower limit for full recovery according to some authors.[32] Previous research already showed that patients may encounter mild symptoms despite rehabilitation,[33 34] and in our opinion this is important to discuss early in rehabilitation to adequately manage patient expectations.

We could not find a significant difference in clinical improvement between the different contraction modes used in our study, and the magnitude of the differences was far below the MCIDs reported for the VISA-A and VAS.[28-30] This corresponds with other studies comparing different loading programmes in AT,[8 11] and studies investigating loading programmes for other tendinopathies,[35-37] and may suggest that contraction mode is not decisive for the effect of loading in AT rehabilitation. Yet, as both programmes include eccentric contractions, it may also be that eccentric loading is the key for clinical improvement, and that adding concentric exercises is of little value. To our knowledge, only one study showed that Alfredson isolated eccentric loading is superior to concentric loading.[38] However, in this study many of the involved concentric exercises were non or partial weightbearing. Obviously, this is less demanding for the muscle-tendon complex than full weightbearing exercises, and therefore, supported by the current findings, we caution against the conclusion that eccentric loading is superior to concentric loading.

Whilst we could not demonstrate significant differences in terms of clinical improvement between the SG and the AG, we found some interesting findings on QOL and perceived effect (GPE). In both groups, QOL improved at one-year follow-up, with fewer participants reporting problems with mobility, usual activities, and pain in both groups. However, in the SG, more problems with anxiety/depression were reported in comparison with the

AG. Somewhat contrary to the latter findings, the number of participants who considered themselves improved after one year (GPE) was significantly larger in the SG than in the AG ($p = 0.04$). This may be explained by the age differences between both groups. Participants in the AG were younger, and since age is suggested to be associated with patient expectations,[39] it can be hypothesized that participants in the AG had higher expectations and consequently were less satisfied with their improvement. However, as the age differences were limited, this explanation remains speculative. Although a firm conclusion cannot be drawn, our findings may indicate that some aspects of improvement are not fully captured by the VISA-A and VAS-scores and that outcome measures evaluating QOL and perceived effects should be included in AT intervention studies.

The strength of our study is its pragmatic nature and the clinical applicability of our design. By solely using home-based exercise interventions with minimal supervision, participants were largely self-responsible for their recovery. The clinically relevant results and the rather high adherence rates found in both groups (i.e. 74.1% and 77.3%) indicate that self-management is an appropriate management strategy for midportion AT, and that intensive supervision may not be required. Whilst it can be argued that more frequent supervision may have improved the adherence rates and thereby could have yielded superior results.

The main limitation of our trial is that we did not reach our targeted sample size, due to unforeseen circumstances and strict exclusion criteria (e.g. regarding duration of symptoms, bilateral symptoms and other musculoskeletal injuries). The latter increased homogeneity of our study sample, but it also impeded to reach the targeted sample size. Consequently, our results are based on less participants than desired. This affects the precision of our estimates and increases the chance of a type II error. Several attempts to increase the inclusion rate unfortunately did not sufficiently affect the final sample size.

We did not include imaging modalities to establish the diagnosis of midportion AT, which may also be recognized as a limitation of our study. Although imaging is not considered necessary for diagnosing AT,[14] it could have been useful in establishing the stage of tendinopathy and ruling out other confounding pathology.

Although we emphasize that our conclusions should be interpreted with caution, we feel that the observed treatment effects still indicate that there are no relevant differences in clinical effects between the included loading programmes. However, future adequately powered studies are warranted to validate this statement and to further explore the relevance of contraction mode in rehabilitation of AT.

Clinical implications

In this study we found that loading according to either the Alfredson and the Silbernagel protocol is effective in reducing clinical symptoms. However, our results did not demonstrate any difference in effects between both programmes. Although underpowered, these findings suggest that contraction mode may not be a relevant factor for the clinical effect, and clinicians can confidently use both programmes in the rehabilitation of their patients with AT.

CONCLUSION

Although both effective in terms of improvement of clinical symptoms, we found no difference in clinical effects between the Alfredson isolated eccentric and the Silbernagel combined concentric-eccentric loading programme up to one-year follow-up. Given the high adherence rates that were found in this RCT, offering either the Alfredson or the Silbernagel programmes as a home-based programme with limited supervision appears to be an effective treatment strategy for midportion AT.

Acknowledgement

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REFERENCES

1. Alfredson H, Pietilä T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26(3):360-66.

2. Sayana M, Maffulli N. Eccentric calf muscle training in non-athletic patients with Achilles tendinopathy. *J Sci Med Sport* 2007;10(1):52-58.

3. Ram R, Meeuwisse W, Patel C, et al. The limited effectiveness of a home-based eccentric training for treatment of Achilles tendinopathy. *Clin Invest Med* 2013;36(4):E197-206.

4. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.

5. Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: A systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.

6. Silbernagel KG, Thomeé R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35(6):897-906.

7. Silbernagel KG, Thomee R, Thomee P, et al. Eccentric overload training for patients with chronic Achilles tendon pain--a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports* 2001;11(4):197-206.

8. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.

9. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001;357(9263):1191-4.

10. Habets B, van Cingel REH, Backx FJG, et al. Alfredson versus Silbernagel exercise therapy in chronic midportion Achilles tendinopathy: study protocol for a randomized controlled trial. *BMC Musculoskelet Disord* 2017;18(1):296.

11. Beyer R, Kongsgaard M, Hougs Kjaer B, et al. Heavy slow resistance versus eccentric training as treatment for Achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2015;43(7):1704-11.

12. Hutchison AM, Evans R, Bodger O, et al. What is the best clinical test for Achilles tendinopathy? *Foot Ankle Surg* 2013;19(2):112-17.

13. Reiman M, Burgi C, Strube E, et al. The utility of clinical measures for the diagnosis of Achilles tendon injuries: a systematic review with meta-analysis. *J Athl Train* 2014;49(6):820-29.

14. Docking SI, Ooi CC, Connell D. Tendinopathy: is imaging telling us the entire story? *J Orthop Sports Phys Ther* 2015;45(11):842-52.

15. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2009;37(3):463-70.

16. Sierevelt I, van Sterkenburg M, Tol H, et al. Dutch version of the Victorian Institute of Sports Assessment-Achilles questionnaire for Achilles tendinopathy: reliability, validity and applicability to non-athletes. *World J Orthop* 2018;9(1):1-6.

17. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

18. Hurst NP, Kind P, Ruta D, et al. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Br J Rheumatol* 1997;36(5):551-59.

19. Gaida JE, Alfredson H, Kiss ZS, et al. Asymptomatic Achilles tendon pathology is associated with a central fat distribution in men and a peripheral fat distribution in women: a cross sectional study of 298 individuals. *BMC Musculoskelet Disord* 2010;11:41.

20. Konor MM, Morton S, Eckerson JM, et al. Reliability of three measures of ankle dorsiflexion range of motion. *Int J Sports Phys Ther* 2012;7(3):279-87.

21. Allen RH, Gross MT. Toe flexors strength and passive extension range of motion of the first metatarsophalangeal joint in individuals with plantar fasciitis. *J Orthop Sports Phys Ther* 2003;33(8):468-78.

22. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10(1):28-55.

23. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41(7):e1-e6.

24. Fitzmaurice GM, Laird NM, Ware J. Applied longitudinal analysis. New York: John Wiley and Sons 2012.

25. Lemmer JT, Hurlbut DE, Martel GF, et al. Age and gender responses to strength training and detraining. *Med Sci Sports Exerc* 2000;32(8):1505-12.

26. Knobloch K, Schreibmueller L, Kraemer R, et al. Gender and eccentric training in Achilles mid-portion tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2010;18(5):648-55.

27. Van Reenen M, Oppe M, Secnik Boye K, et al. EuroQol Research Foundation. EQ-5D-3L User Guide. Available from: https://euroqol.org/publications/user-guides, 2018.

28. Macdermid JC, Silbernagel KG. Outcome evaluation in tendinopathy: foundations of assessment and a summary of selected measures. *J Orthop Sports Phys Ther* 2015;45(11):950-64.

29. Murphy M, Rio E, Debenham J, et al. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: a review of outcome measures for self- reported pain and function. *Int J Sports Phys Ther* 2018;13(2):283-92.

30. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 2005;14(7):798-804.

31. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: A randomized controlled trial. *Am J Sports Med* 2007;35(3):374-83.

32. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med* 2011;45(5):421-28.

33. van der Plas A, de Jonge S, de Vos RJ, et al. A 5-year follow-up study of Alfredson's heel-drop exercise programme in chronic midportion Achilles tendinopathy. *Br J Sports Med* 2012;46(3):214-18.

34. Silbernagel KG, Brorsson A, Lundberg M. The majority of patients with Achilles tendinopathy recover fully when treated with exercise alone: a 5-year follow-up. *Am J Sports Med* 2011;39(3):607-13.

35. Kongsgaard M, Qvortrup K, Larsen J, et al. Fibril morphology and tendon mechanical properties in patellar tendinopathy: effects of heavy slow resistance training. *Am J Sports Med* 2010;38(4):749-56.

36. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports* 2009;19(6):790-802.

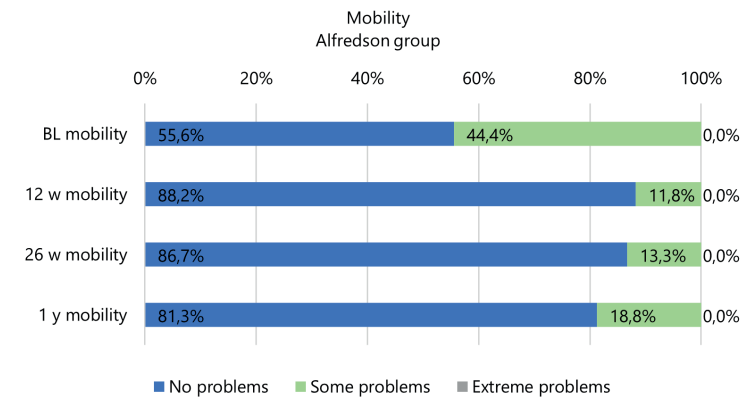
37. Dejaco B, Habets B, van Loon C, et al. Eccentric versus conventional exercise therapy in patients with rotator cuff tendinopathy: a randomized, single blinded, clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2017;25(7):2051-59.

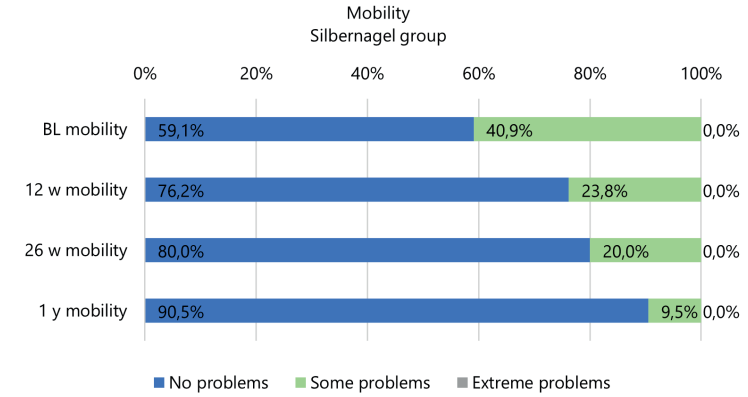
38. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. K*nee Surg Sports Traumatol Arthrosc* 2001;9(1):42-47.

39. Jaworski M, Rzadkiewicz M, Adamus M, et al. Primary care patients' expectations regarding medical appointments and their experiences during a visit: does age matter? *Patient Prefer Adherence* 2017;11:1221-33.

SUPPLEMENTARY MATERIAL

Appendix 4.1 (A-E) Proportions of participants reporting 'no problems', 'some problems' or 'extreme problems' on the subscales mobility (A), self-care (B), usual activities (C), pain/discomfort (D), and anxiety/depression (E) of the EQ-5D questionnaire





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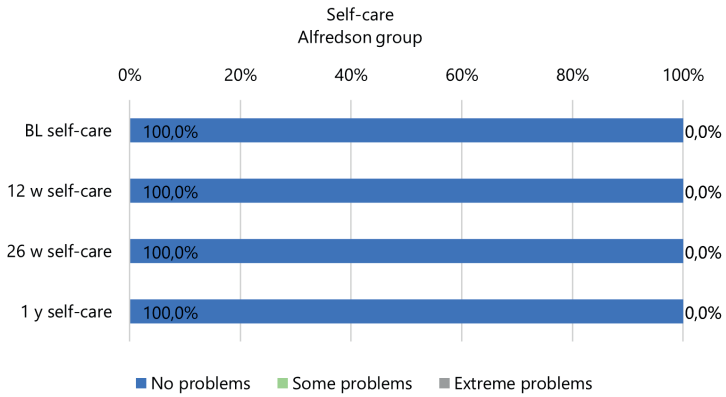
Self-care
Alfredson group
0%
20%
40%
60%
80%
100%
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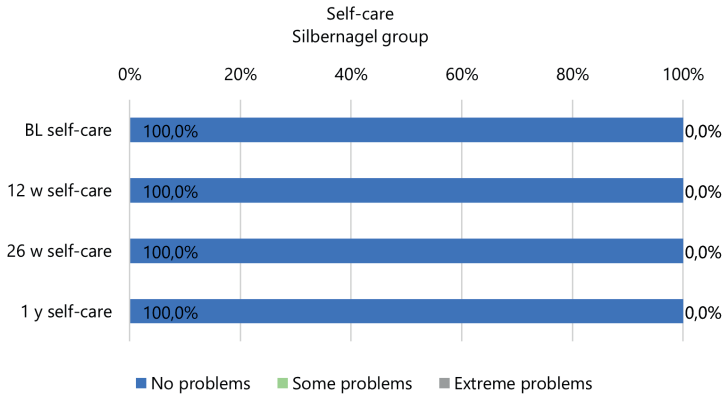
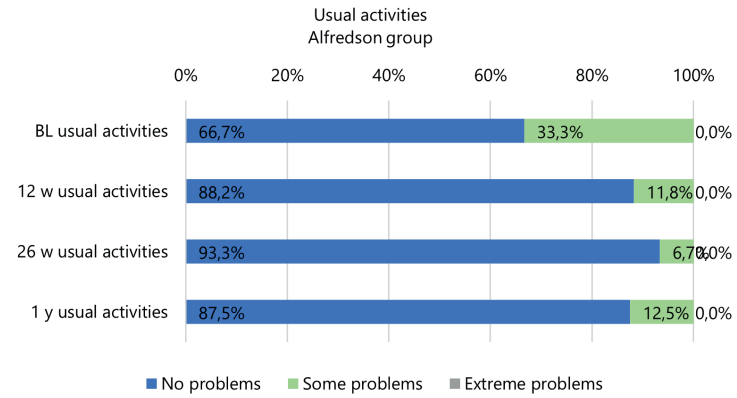
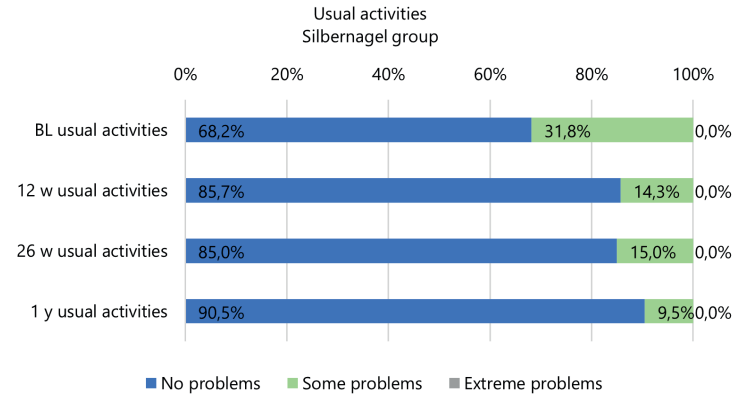
12 w self-care
26 w self-care
1 y self-care
100,0%
0,0%
No problems
Some problems
Extreme problems

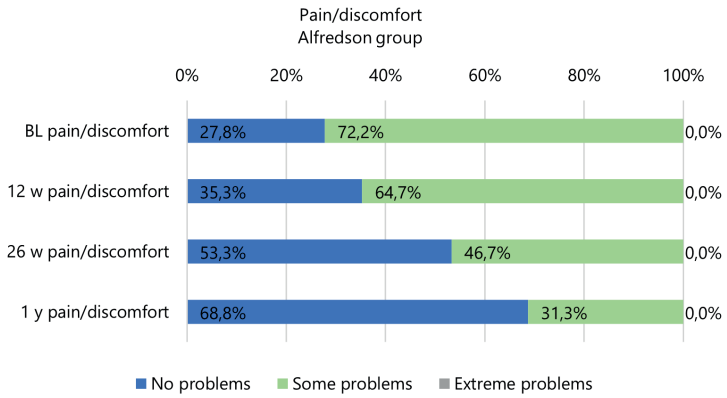

Self-care
Silbernagel group
0%
20%
40%
60%
80%
100%
BL self-care
12 w self-care
26 w self-care
1 y self-care
100,0%
0,0%
No problems
Some problems
Extreme problems

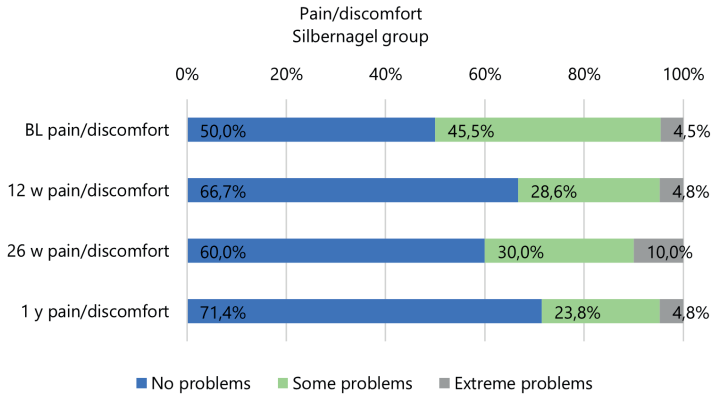
4.1B


Usual activities
Alfredson group
0%
20%
40%
60%
80%
100%
BL usual activities
12 w usual activities
26 w usual activities
1 y usual activities
66,7%
33,3%
88,2%
11,8%
93,3%
6,7%
87,5%
12,5%
0,0%
No problems
Some problems
Extreme problems

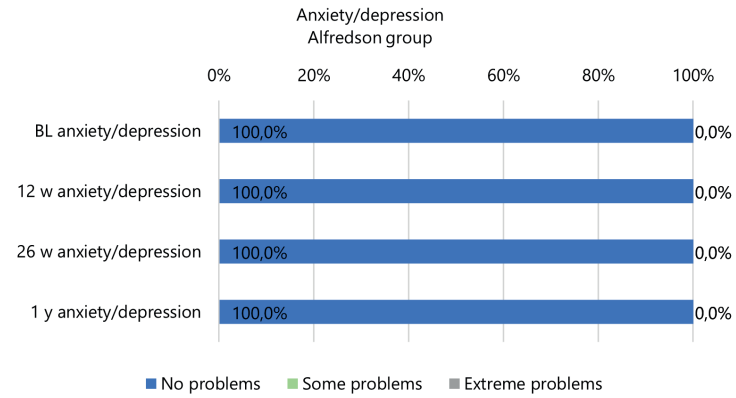

Usual activities
Silbernagel group
0%
20%
40%
60%
80%
100%
BL usual activities
12 w usual activities
26 w usual activities
1 y usual activities
68,2%
31,8%
85,7%
14,3%
85,0%
15,0%
90,5%
9,5%
0,0%
No problems
Some problems
Extreme problems

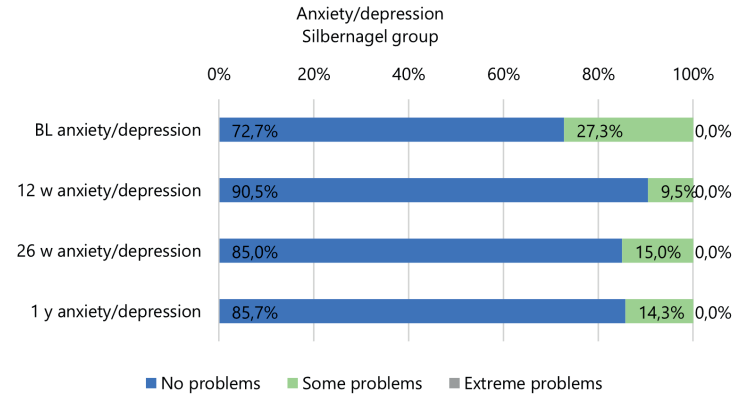
4.1C


Pain/discomfort
Alfredson group
0%
20%
40%
60%
80%
100%
BL pain/discomfort
27,8%
72,2%
0,0%
12 w pain/discomfort
35,3%
64,7%
0,0%
26 w pain/discomfort
53,3%
46,7%
0,0%
1 y pain/discomfort
68,8%
31,3%
0,0%
No problems
Some problems
Extreme problems


Pain/discomfort
Silbernagel group
0%
20%
40%
60%
80%
100%
BL pain/discomfort
50,0%
45,5%
4,5%
12 w pain/discomfort
66,7%
28,6%
4,8%
26 w pain/discomfort
60,0%
30,0%
10,0%
1 y pain/discomfort
71,4%
23,8%
4,8%
No problems
Some problems
Extreme problems

4.1D


Anxiety/depression
Alfredson group
0%
20%
40%
60%
80%
100%
BL anxiety/depression
100,0%
0,0%
12 w anxiety/depression
100,0%
0,0%
26 w anxiety/depression
100,0%
0,0%
1 y anxiety/depression
100,0%
0,0%
No problems
Some problems
Extreme problems


Anxiety/depression
Silbernagel group
0%
20%
40%
60%
80%
100%
BL anxiety/depression
72,7%
27,3%
0,0%
12 w anxiety/depression
90,5%
9,5%
0,0%
26 w anxiety/depression
85,0%
15,0%
0,0%
1 y anxiety/depression
85,7%
14,3%
0,0%
No problems
Some problems
Extreme problems

4.1E

CHAPTER 5

Alfredson versus Silbernagel loading in recreational athletes with midportion Achilles tendinopathy: a randomised controlled trial comparing functional performance of the lower extremity and return to sport

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Under review.

ABSTRACT

Purpose: To test for differences in effects on functional performance and return to sport (RTS) rate at one-year follow-up between the Alfredson and the Silbernagel programme in midportion Achilles tendinopathy (AT).

Methods: A randomised clinical trial was performed. Forty recreational athletes were allocated to the Alfredson (AG, n = 18) or the Silbernagel group (SG, n = 22). At baseline, 12-week and one-year follow-up, participants performed the heel-raise test for evaluating plantar flexor endurance, the single leg countermovement jump (CMJ) to evaluate reactive strength of the plantar flexor complex, and isometric strength measurements of the hip abductors, extensors and external rotators. At one-year follow-up we assessed the RTS rate. Analysis was performed with a linear mixed model with intervention, time and intervention-by-time interaction.

Results: The intervention-by-time interaction did not improve the model. Hence, we report a treatment effect (AG as reference) without interaction term, indicating a constant difference at each follow-up. Plantar flexor endurance significantly improved from baseline to one-year (AG: 24.2±8.4 to 30.1±10.0 repetitions, SG: 25.4±8.7 to 29.8±10.9), but after correction for baseline values and confounders, a non-significant treatment effect was found (2.7, 95% CI [-0.5, 5.9], *P*=0.092). Hip external rotator strength significantly improved in both groups from baseline to one-year follow-up. Nonetheless, after adjustment for respective baseline measurements and confounders, non-significant treatment effects were found for the CMJ (-0.4, 95% CI [-1.6, 0.8], *P* = 0.481), and all hip muscle strength tests (extensors: -0.1, 95% CI [-0.4, 0.1], *P*=0.262; abductors: -0.2, 95% CI [-0.5, 0.1], *P*=0.195; external rotators: -0.1, 95% CI [-0.2, 0.0], *P*=0.193). After one year, RTS rate in the SG was 80% higher than in the AG (68% vs. 38%), but this difference was non-significant (*P*=0.104).

Conclusion: We found meaningful improvement of plantar flexor endurance and hip external rotator strength up to one-year follow-up after the Alfredson and the Silbernagel programme. No significant differences were found between both programmes. Jump height and hip extensor en abductor strength did not significantly improve and no differences between the groups were found. At one-year follow-up, RTS rate in the SG was more than 80% higher.

INTRODUCTION

Midportion Achilles tendinopathy (AT) is one of the most prevalent lower extremity overuse injuries in sports.[1] Although strong evidence for a causal relationship is lacking,[2 3] AT is associated with impaired functional performance of the plantar flexor muscle-tendon complex. For example, decreased strength and endurance of the plantar flexors is frequently found in patients with AT,[4-6] and research also reports altered plantar flexor activation patterns in runners with AT.[7] Functional performance deficits in those with AT may even extend throughout the proximal lower extremity, with studies demonstrating diminished strength and neuromuscular control of the hip musculature compared with asymptomatic controls,[8-10] and altered stretch-shortening cycle behavior during submaximal hopping.[11] This indicates that functional performance of the entire lower extremity may be affected in patients with AT.

In the last decades, progressive loading of the plantar flexors has become the mainstay for treating AT. Traditionally, the Alfredson isolated eccentric loading programme, which comprises 12 weeks of the same eccentric heel-lowering exercises performed twice daily, is most frequently used, with comprehensive evidence supporting its effect on clinical symptoms.[12-14] The Silbernagel programme, which involves a combination of various concentric-eccentric exercises, is used less often, but has also demonstrated promising results in terms of clinical improvement.[15 16]

Although both programmes have shown improvement on clinical symptoms, effects on functional performance may be less. Silbernagel et al. showed that functional performance of the lower extremity – evaluated with a test battery including measurements for plantar flexor strength and endurance, and various jump tests – was not automatically restored following their loading programme, even though symptoms had fully subsided.[17] In our opinion, this highlights the need for incorporating an evaluation of functional performance of the lower extremity in intervention studies on AT, as decreased functional performance may put an athlete at risk for re-injury when sports activities are resumed. However, research on the effects of both the Alfredson and Silbernagel programme on functional performance is scarce,[18] and comparison between both programmes is lacking. Therefore, the present study aimed to test for differences in effects on functional performance between the Alfredson and Silbernagel loading programme in a randomised controlled trial (RCT) with one-year follow-up.

MATERIALS AND METHODS

Study design and setting

A single-blind RCT was conducted, with the University Medical Center Utrecht and Sports Medical Center Papendal as participating centers. Because of an unforeseen slow inclusion

rate, three private clinics for physiotherapy (Academie Instituut, FysioHolland Medicort, and Van Tongeren Fysiotherapie) were added to facilitate enrollment of participants. A detailed description of this RCT can be found in the study protocol.[19]

Participants were randomised to 12 weeks of eccentric loading according to the original Alfredson programme,[20] or a combination of concentric and eccentric loading in accordance with the Silbernagel programme.[21 22] Exercises from both programmes were performed at home, but participants had three sessions with a supervising physiotherapist from one of the participating centers. The objective of these supervision sessions was adequate exercise instruction and adjustment of the exercises according to the protocol when possible. To ensure uniformity of participant instruction, all supervising physiotherapists were given standardized written and oral instructions on the exercise programmes prior to the study. Due to the nature of the intervention, both participants and supervising physiotherapists could not be blinded to the allocated programme. Research staff involved in collecting, entering and analyzing the data was not involved in any of the interventions and was blinded to group allocation.

The RCT was prospectively registered in the Dutch Trial Register (NTR5638), and the local ethical committee of the University Medical Center Utrecht approved the design and informed consent procedure (16-158/M).

Study population

Men and women diagnosed with chronic (i.e ≥ 3 months) unilateral midportion AT, aged between 18-65 years, were eligible for inclusion in this RCT if they participated in sports involving Achilles tendon loading. The diagnosis of midportion AT was confirmed by the main researcher (BHa), based on subjective and palpation pain in the Achilles tendon, 2-7 cm proximal to the calcaneal insertion,[23] swelling, and subjective stiffness during the first steps in the morning.[24] Potential participants were excluded if they had bilateral symptoms, were diagnosed with insertional AT, received other treatments in the last four weeks, underwent a corticosteroid injection in the region of the Achilles tendon in the previous 12 months, suffered from other lower limb injuries or underwent surgery of the affected limb in the previous 12 months, had a history of Achilles tendon rupture in the affected limb, or had systemic diseases potentially interfering with their recovery (e.g. rheumatoid arthritis or diabetes mellitus).

Recruitment and randomisation

Sports medicine physicians, general practitioners, and physiotherapists recruited the participants for this study. Participants were initially screened by telephone by the main researcher (BHa) and received an information letter. If they met the eligibility criteria and wanted to participate, an appointment for baseline assessment was made with the main researcher (BHa). Prior to the baseline assessment, participants signed informed consent. After baseline assessment, an independent secretary performed the randomisation by

choosing an envelope from a box with opaque sealed envelopes, which were consecutively numbered according to a computer-generated randomisation table. Subsequently, participants were scheduled for an intake with one of the supervising physiotherapists from the participating centers. Prior to the intake, the secretary who performed the randomisation, communicated to the supervising physiotherapist which loading programme should be followed.

Loading programmes

Both loading programmes were performed at home. Participants in the Alfredson group (AG) performed 12 weeks of eccentric heel-lowering exercises on the edge of a stair, using the non-injured limb to concentrically return to the starting position.[20] In the Silbernagel group (SG), participants performed 12 weeks of concentric-eccentric loading, divided into three phases.[21] Details of the programmes are given in Table 5.1.
During the intake, the allocated programme was explained in detail by the supervising physiotherapist, so that participants could correctly perform the exercises at home. Two and six weeks later, an appointment with the same supervising physiotherapist was scheduled to adequately adjust exercises and load according to the protocol. During the 12-week exercise period, no additional treatments were given. Participants were asked not to engage in tendon-loading sports activities during the first three weeks of the programme. Thereafter, they were advised to resume sports activities, provided that pain during activity did not exceed 5 on a 0-10 numerical rating scale, and symptoms subsided within 24 h after the respective activity.[21]

Table 5.1 Key features of the loading programmes

	Alfredson programme	**Silbernagel programme**
Duration of programme	12 weeks	12 weeks
Frequency of exercises	Twice daily	Once daily
Number of exercises	2	4-5
Sets and repetitions	3x15	3x15
Contraction mode	Slow isolated eccentric	Concentric-eccentric, eccentric, quick-rebounding, plyometric
Pain	Acceptable if non-disabling pain	Acceptable if no more than 5 on a 0-10 numerical rating scale
Criteria for progression	When exercises can be performed without pain/discomfort	No increase of symptoms Phase 1: weeks 1-2 Phase 2: weeks 2-5 Phase 3: weeks 3-12
Load	Add load in steps of 5 kg	Add load in steps of 5 kg

Measurements

Demographic and anthropometric baseline data collected were age, sex, body height/weight and duration of symptoms. Additionally, several clinical data were collected: waist circumference,[25] ankle dorsiflexion range of motion using the weight bearing lunge test,[26] and extension range of motion of the first metatarsophalangeal joint measured with a goniometer.[27]

Outcome assessment was performed at baseline, at 12-week, and at one-year follow-up by one researcher (BHa), who was blinded for the allocated treatment. Functional performance was assessed with the heel-raise test, the countermovement jump (CMJ), isometric strength tests of the hip extensors, abductors and external rotators, and the return to sport (RTS) rate. Tests were performed in the same order, always starting with the uninjured limb and then the injured limb. Each test was separated by 2 min of rest to minimize variation in results due to fatigue. Participants performed no specific warming-up prior to the tests, but after verbal instruction of the test procedure, they were allowed 3 to 5 trial repetitions to become familiar with the movement.

Heel-raise test

Endurance of the plantar flexors was measured using the heel-raise test, which is considered a valid and reliable test for this purpose.[28 29] Participants were asked to stand on one leg, with their fingertips against the wall for balance support. Subsequently, they were instructed to perform as many heel-raises as possible (as high as possible for every raise), with their knee straight and a frequency of 30 raises per minute. The test was discontinued when the participant had to stop due to exhaustion, could not keep the frequency, or the technique was incorrect for two consecutive repetitions (e.g. knee flexion).[30] The total number of correct heel-raises was registered and used for data analysis.

CMJ

The single-leg CMJ was included to assess reactive strength of the plantar flexor muscle-tendon complex.[31] The CMJ was performed with the participant standing on one leg in an upright position on a jumping platform (ProJump, Biometrics, The Netherlands).[32] The hands were placed behind the back, and subsequently, participants were instructed to squat down as much as they wanted, and then immediately jump upwards to maximum height. For each limb, three trial repetitions were allowed, followed by three consecutive test repetitions. Each jump was separated by 30 sec of rest. The highest jump was used for data analysis.[22]

Isometric strength of the hip abductors, extensors and external rotators

As research has demonstrated strength of the proximal muscle groups of the lower extremity may be decreased in patients with AT, we also included isometric strength measurements of the hip abductors, extensors and external rotators to evaluate functional performance of the proximal lower extremity.[33] The hip abductors were measured with the

participant in side-lying position, the hip extensors were measured in prone position, and for the external rotators, participants were sitting on an examination table with their hips and knees flexed to 90° and their hands placed behind their back.[8 33] For the isometric strength tests, two submaximal trial repetitions were allowed, and subsequently, three test repetitions were performed, separated by 30 sec of rest. The best repetition for each muscle group was used for data analysis.

RTS rate

Besides the physical tests, we evaluated the proportion of participants who were able to successfully return to their pre-injury sports level at one-year follow-up (i.e. RTS rate).[34] To this end, participants completed a questionnaire regarding their current sports activities, i.e. type of sport and time spent (hrs/wk) in the week prior to assessment. We used a self-developed ordinal scale to categorize type of sport, based on the theoretical assumption that higher categories would be more demanding in terms of Achilles tendon load. The categories were: 1) no present sport activity, 2) cycling or fitness, 3) walking; 4) running, and 5) ball sports.

Statistical analyses

Statistical analysis was performed according to intention-to-treat principle, with significance level (two-sided) set at $P \leq 0.05$, using SPSS 23.0. An a priori sample size calculation was performed, with $\alpha = 0.05$ and 80% power, resulting in a required sample size of 86 participants (i.e. 43 in both groups).[19] Prior to analysis, strength tests of the hip musculature were corrected for body weight by dividing the peak value of the best repetition by the body weight at the time of the respective measurement (i.e. N/kg). Furthermore, normality of the data was examined, and a graphical representation of observed mean scores and 95% confidence intervals (CIs) was composed for the outcome measures. Patient characteristics were presented as means±SD or numbers (percentage). We used a paired t-test to compare baseline values of the physical tests between the injured and non-injured limb. In line with current recommendations, statistical comparison of baseline characteristics between the groups was not performed.[35]

Due to missing data in follow-up measurements, the heel-raise test, CMJ and the hip muscle strength tests at follow-up were analyzed with a linear mixed model, instead of the repeated measures ANOVA that we planned to use.[19] The model included an unstructured residual covariance (GEE type) to adjust for repeated measurements within the same participants.

We initially used a model that included intervention (AG versus SG), time (i.e. 12 and 52 weeks) and intervention-by-time interaction. Subsequently, the intervention-by-time interaction effect was evaluated and tested with likelihood ratio tests for all outcomes. In case the interaction did not significantly improve any model fit, it was excluded from the final analysis. Validity of the model was assessed using residual analyses.[36]

The heel-raise test, the CMJ, and the strength tests of the hip extensors, abductors and external rotators during follow-up were included as dependent variables, and the baseline value of the respective outcome was included as covariate. Additionally, sex, age, and duration of symptoms were included as covariates, since these were considered potential confounders.[37 38]

In agreement with our study aim (i.e. to test for differences in effects on functional performance, with the AG as reference), we present the treatment effect (95% CI) at one-year follow-up, with adjustment for baseline and confounders, but without the intervention-by-time interaction. For completeness, we also report the results for all models, i.e. the initial model (intervention, time and intervention-by-time interaction), the model with correction for baseline, and the model with correction for baseline and confounders. Differences between the programmes were reported as differences in the mean with 95% CI and corresponding *P*-values.

To assess whether participants had successfully returned to their previous sports level at one- year follow-up, RTS was dichotomized into 'successful' or 'non-successful'. Successful RTS was met if participants had returned to the same category or higher compared to baseline, and the weekly time spent (h/wk) was similar or higher compared to baseline.[34] If either type or weekly time spent at one-year follow-up were less than baseline level, it was defined as non-successful RTS. Difference in RTS rate between the groups was analyzed with the Pearson's X^2 test.

RESULTS

Since we encountered difficulty in recruiting sufficient participants, and due to the outbreak of COVID-19, enrollment of participants was terminated in April 2020, before reaching the intended sample size. Planned follow-up measurements after this date were performed as scheduled. Between December 2016 and April 2020, a total of 40 participants were included. Two participants in the AG, and one participant in the SG were lost to follow-up (see Figure 5.1). Their data were included in the analysis.

Baseline characteristics of the study population

Table 5.2 shows the baseline characteristics of the participants. The groups were not perfectly balanced, probably due to the small sample size, with differences observed for example regarding age, duration of symptoms and type of sport.

For the heel-raise test, the injured limb performed significantly worse compared to the non-injured limb in both groups (Table 5.2; AG: $P = 0.001$; SG: $P = 0.002$). Performance of the injured and non-injured limb on the CMJ and the hip muscle strength tests did not significantly differ (Table 5.2).

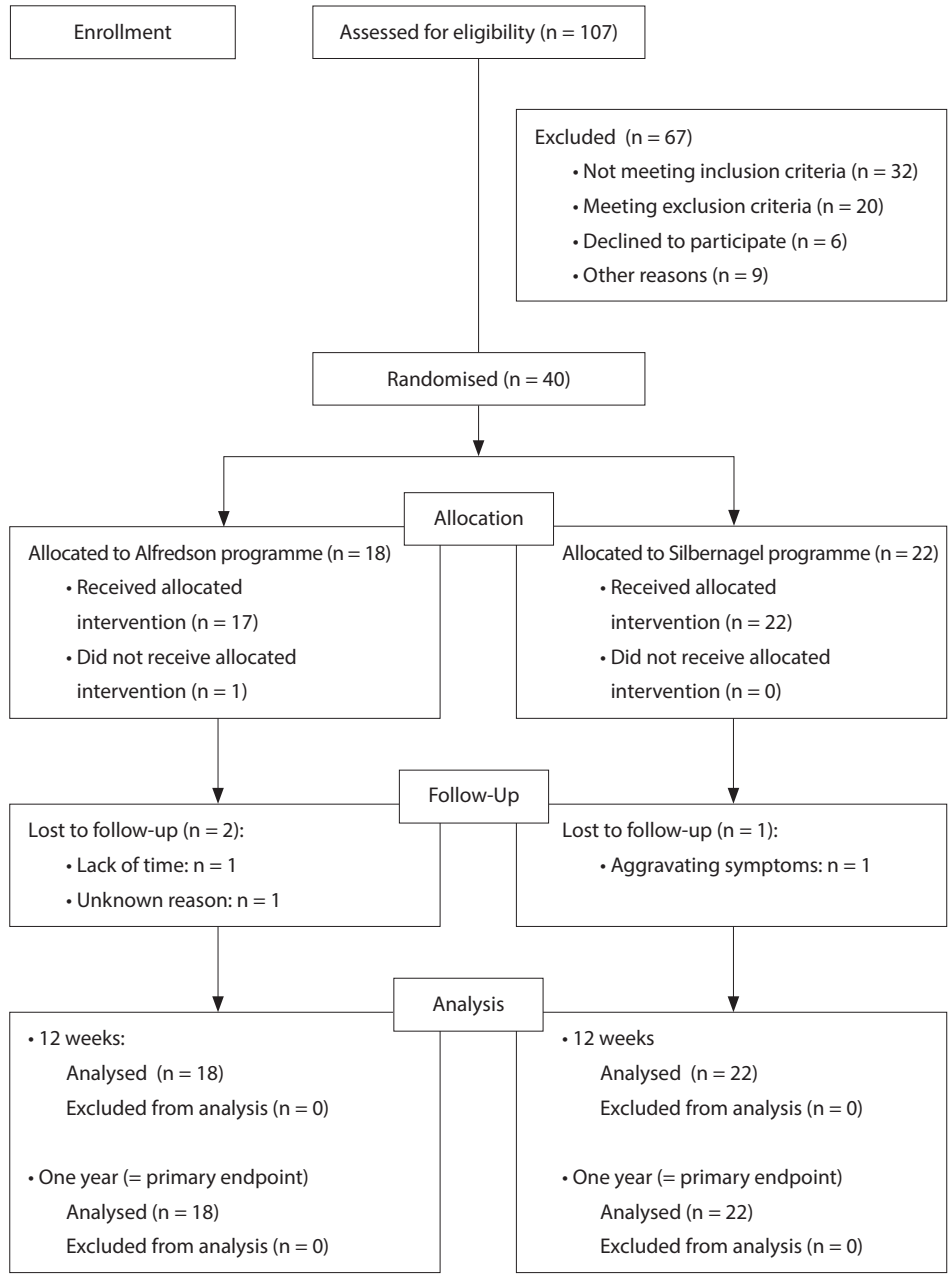


Figure 5.1 Flow chart of the study population throughout the study

Table 5.2 Baseline characteristics of study population

	Alfredson group (n = 18)	*P*-value[b]	Silbernagel group (n = 22)	*P*-value[b]
Sex (%)	8 female (44.4%)	n/a	10 female (47.6%)	n/a
Age (years)[a]	44.7±9.0	n/a	49.9±10.1	n/a
Height (cm)[a]	179.7±8.6	n/a	175.4±9.8	n/a
Weight (kg)[a]	84.7±15.6	n/a	81.3±15.4	n/a
BMI (kg/cm^2)[a]	26.1±3.	n/a	26.3±4.1	n/a
Injured limb N (%)	12 left (66.7%)	n/a	11 left (50.0%)	n/a
Duration of symptoms (months)[a]	9.4±8.2	n/a	15.1±24.0	n/a
Sport type N (%)				
- No current sport	-	n/a	2 (9.1%)	n/a
- Cycling/fitness	-		1 (4,5%)	
- Walking	8 (44.4%)		6 (27.3%)	
- Running	1 (5.6%)		6 (27.3%)	
- Ball sports	9 (50.0%)		7 (31.8%)	
Weekly time spent on sport (h)[a]	4.7±4.7	n/a	5.1±3.5	n/a
Waist circumference (cm)[a]	94.3±11.5	n/a	94.8±12.6	n/a
ROM dorsiflexion TCJ (cm)[a]				
- Injured limb	12.4±3.0	0.797	10.5±2.6	0.435
- Non-injured limb	12.5±3.7		10.1±3.5	
ROM dorsiflexion MTP1 (°)[a]				
- Injured limb	44.7±14.2	0.266	43.1±10.9	0.668
- Non-injured limb	46.2±13.8		43.6±11.2	
Heel raise test (count)[a]				
- Injured limb	24.2±8.4	0.001[c]	25.4±8.7	0.002[c]
- Non-injured limb	29.8±8.7		29.0±8.0	
CMJ (cm)[a]				
- Injured limb	9.8±4.7	0.160	9.0±4.5	0.794
- Non-injured limb	10.6±5.5		8.8±4.2	
HHD hip extensors (N/kg)[a]				
- Injured limb	2.8±0.8	0.704	2.9±0.9	0.066
- Non-injured limb	2.8±0.8		3.1±1.0	
HHD hip abductors (N/kg)[a]				
- Injured limb	3.1±0.9	0.955	3.1±0.8	0.395
- Non-injured limb	3.2±0.9		3.2±0.8	
HHD hip external rotators (N/kg)[a]				
- Injured limb	2.1±0.7	0.548	2.0±0.4	0.334
- Non-injured limb	2.2±0.6		2.0±0.4	

BMI = body mass index; *ROM* = range of motion; *TCJ* = talocrural joint; *MTP1* = first metatarsophalangeal joint; *CMJ* = countermovement jump; *HHD* = hand-held dynamometer
[a] data reported as mean±standard deviation
[b] *P*-values for comparison between the injured and non-injured limb using a paired t-test
[c] Significant difference between the injured and non-injured limb at $P \leq 0.05$ level

Follow-up measurements

Figure 5.2 graphically shows the observed mean values with 95% CIs of the heel raise test (A-B), the CMJ (C-D), and the strength tests of the hip musculature (E-J). Table 5.3 shows the treatment effects for each follow-up measurement (AG as reference), unadjusted and with adjustment for baseline and confounders.

Heel-raise test

The heel-raise test of the injured limb significantly increased from 24.2±8.4 to 30.1±10.0 repetitions (Figure 5.2A, $P = 0.050$) at one-year follow-up in the AG, and from 25.4±8.7 to 29.8±10.9 repetitions in the SG ($P = 0.050$). Mixed model analysis without intervention-by-time interaction showed a non-significant treatment effect after correction for baseline heel-raise test and confounders (2.7, 95% CI [-0.5, 5.9], $P = 0.092$).

CMJ

In the AG, the CMJ of the injured limb showed an average improvement of 0.6 cm from baseline to one-year follow-up (9.8±4.7 cm to 10.4±5.4, $P = 0.154$). For the SG, improvement was 1.6 cm (9.0±4.5 to 10.6±5.2, $P = 0.154$). After adjustment for baseline CMJ and confounders, a non- significant treatment effect was found (-0.4, 95% CI [-1.6, 0.8], $P = 0.481$).

Isometric strength of the hip abductors, extensors and external rotators

All hip muscle groups of the injured limb showed improved strength at one-year follow-up, but only for the hip external rotators this improvement was statistically significant ($P = 0.029$).

Linear mixed model analysis with correction for baseline strength measurements and confounders showed non-significant treatment effects for any of the hip muscle groups (extensors: -0.1, 95% CI [-0.4, 0.1], $P = 0.262$; abductors: -0.2, 95% CI [-0.5, 0.1], $P = 0.195$; external rotators: -0.1, 95% CI [-0.2, 0.0], $P = 0.193$).

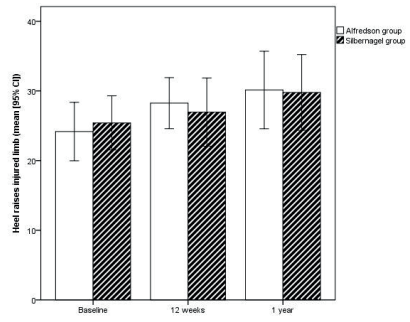
RTS rate

At baseline, the average weekly time spent on sport was 4.7±4.7 h for the AG and 5.1±3.5 h for the SG. A difference was observed between the groups in the proportion of participants participating in the different sports categories (particularly for running, see Table 5.2). At one-year follow-up, the average weekly time spent on sport for the AG was 4.3±5.0 h and for the SG 5.4±3.1 h. RTS rate in the AG was 37.5%, and 67.7% in the SG. This difference was not statistically significant ($P = 0.104$).

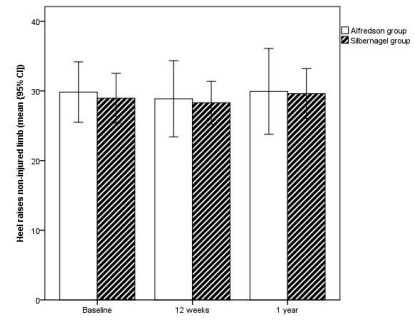
Table 5.3 Treatment effects in the injured and non-injured limb between the Alfredson and the Silbernagel group

	Without correction		With correction for baseline		With correction for baseline and confounders[a]	
	Treatment effect[b] (95% CI)	***P*-value**	**Treatment effect[b] (95% CI)**	***P*-value**	**Treatment effect[b] (95% CI)**	***P*-value**
			Injured limb			
Heel-raise test (repetitions)						
12 weeks	1.3 (-4.7, 7.3)	0.662	2.9 (-0.9, 6.7)	0.127	2.8 (-0.9, 6.5)	0.136
1 year	1.7 (-5.5, 8.9)	0.638	2.8 (-2.0, 7.6)	0.242	2.6 (-1.8, 7.0)	0.241
CMJ (cm)						
12 weeks	0.1 (-2.8, 3.0)	0.945	-0.2 (-1.4, 1.0)	0.737	-0.4 (-1.6, 0.8)	0.466
1 year	0.5 (-2.9, 4.0)	0.763	0.2 (-1.5, 1.9)	0.824	-0.1 (-1.7, 1.6)	0.951
HHD hip extensors (N/kg)						
12 week	-0.2 (-0.7, 0.3)	0.435	-0.1 (-0.4, 0.2)	0.502	-0.2 (-0.4, 0.1)	0.255
1 year	0.3 (-0.5, 1.0)	0.465	0.3 (-0.2, 0.9)	0.184	0.3 (-0.3, 0.8)	0.296
HHD hip abductors (N/kg)						
12 weeks	-0.1 (-0.6, 0.5)	0.828	-0.1 (-0.5, 0.2)	0.451	-0.2 (-0.6, 0.1)	0.234
1 year	0.1 (-0.6, 0.7)	0.784	-0.0 (-0.5, 0.4)	0.836	-0.1 (-0.6, 0.3)	0.504
HHD hip external rotators (N/kg)						
12 weeks	0.0 (-0.3, 0.4)	0.910	-0.1 (-0.2, 0.1)	0.226	-0.1 (-0.2, 0.1)	0.297
1 year	-0.0 (-0.3, 0.3)	0.992	-0.2 (-0.4, 0.0)	0.107	-0.1 (-0.3, 0.1)	0.165
			Non-injured limb			
Heel-raise test (repetitions)						
12 weeks	0.1 (-5.3, 5.5)	0.975	0.4 (-2.9, 3.6)	0.822	0.0 (-3.3, 3.4)	0.978
1 year	0.4 (-5.6, 6.4)	0.891	0.6 (-4.4, 5.6)	0.809	0.3 (-4.5, 5.1)	0.903
CMJ (cm)						
12 weeks	0.6 (-2.2, 3.4)	0.673	-0.8 (-2.1, 0.5)	0.203	-1.1 (-2.3, 0.0)	0.058
1 year	1.1 (-1.9, 4.1)	0.459	-0.4 (-1.3, 0.6)	0.439	-0.7 (-1.6, 0.2)	0.111
HHD hip extensors (N/kg)						
12 weeks	-0.2 (-0.8, 0.3)	0.410	-0.0 (-0.3, 0.2)	0.943	-0.0 (-0.3, 0.2)	0.774
1 year	0.1 (-0.5, 0.8)	0.665	0.4 (0.0, 0.7)	0.039	0.3 (-0.0, 0.7)	0.065
HHD hip abductors (N/kg)						
12 weeks	-0.1 (-0.6, 0.5)	0.790	-0.0 (-0.4, 0.3)	0.946	-0.0 (-0.4, 0.3)	0.849
1 year	0.0 (-0.5, 0.5)	0.920	0.0 (-0.3, 0.4)	0.899	-0.0 (-0.4, 0.3)	0.995
HHD hip external rotators (N/kg)						
12 weeks	-0.0 (-0.4, 0.3)	0.866	-0.1 (-0.3, 0.1)	0.205	-0.2 (-0.3, 0.0)	0.108
1 year	-0.0 (-0.3, 0.3)	0.975	-0.1 (-0.3, 0.1)	0.359	-0.1 (-0.3, 0.1)	0.210

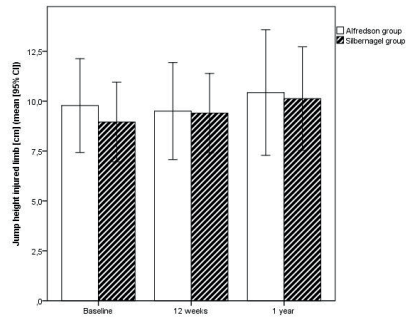
CI = confidence interval; *CMJ* = countermovement jump; *HHD* = hand-held dynamometer
[a] Baseline measurement of respective outcome, sex, age, and duration of symptoms
[b] Treatment effects are reported as differences in means with the Alfredson group as reference group



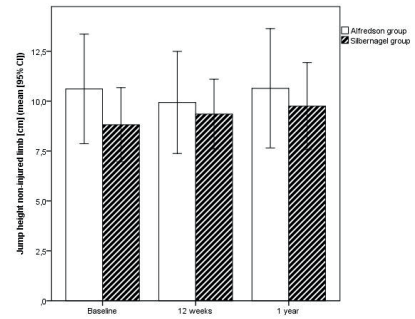
2A. Heel-raise test injured limb



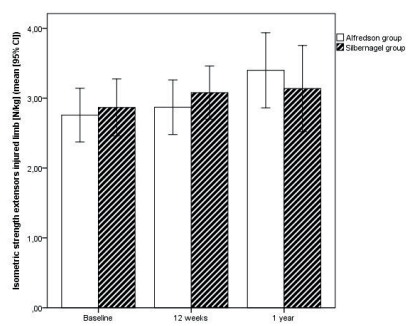
2B. Heel-raise test non-injured limb



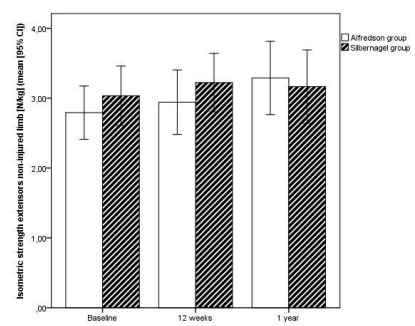
2C. Countermovement jump injured limb



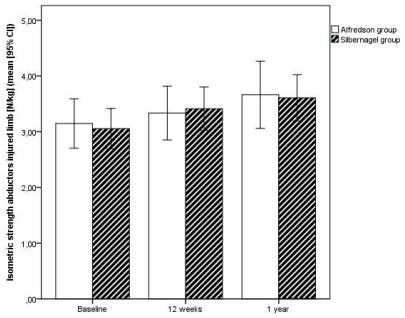
2D. Countermovement jump non-injured limb



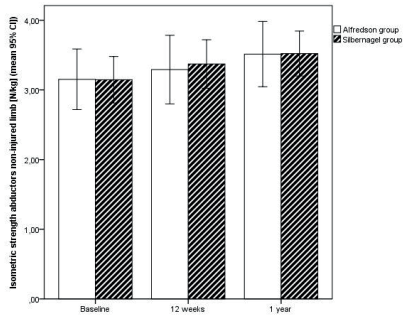
2E. Isometric strength hip extensors injured limb



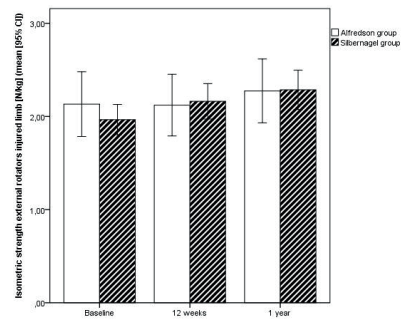
2F. Isometric strength hip extensors non-injured limb



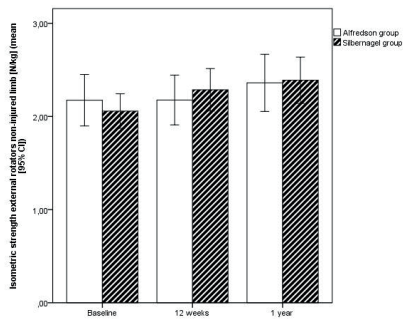
2G. Isometric strength hip abductors injured limb



2H. Isometric strength hip abductors non-injured limb



2I. Isometric strength hip external rotators injured limb



2J. Isometric strength hip external rotators non-injured limb

Figure 5.2 (A-J) Observed progression of the heel-raise test, the countermovement jump and the isometric strength tests of the hip musculature from baseline to one-year follow-up

DISCUSSION

This is the first RCT comparing effects on functional performance of the Alfredson and the Silbernagel loading programme in midportion AT. In a sample of recreational athletes, we found that both programmes significantly improved plantar flexor muscular endurance up to one-year follow-up, but without significant differences between the programmes. Also, no significant difference between the programmes was found for jump height (CMJ) and isometric hip muscle strength. At one-year follow-up, the RTS rate in the SG was considerably higher than in the AG, but this difference was not statistically significant.

Effects on functional performance of both programmes have previously been investigated. Alfredson et al. described significantly improved plantar flexor strength immediately following their loading programme.[20 39] For the Silbernagel programme, research showed that clinical improvement is associated with improved endurance of the plantar flexors,[22] improved jump performance,[22] and increased calf muscle power,[21] but the strength of this evidence is moderate at best.[15]

As recommended in a recent guideline,[16] we included a measure for evaluating plantar flexor endurance. According to a recent review, the heel-raise test is an appropriate clinical test for this purpose.[40] In our study, both groups demonstrated decreased plantar flexor endurance in the injured limb compared to the non-injured limb at baseline, whilst Silbernagel et al. suggested that the heel-raise test is not capable of revealing a difference between the injured and non-injured (or least symptomatic) limb.[32] A possible explanation is that Silbernagel et al. also included participants with bilateral symptoms,[32] whereas we solely included participants with unilateral symptoms. Differences in plantar flexor endurance are hypothetically more pronounced when the injured limb is compared to an asymptomatic limb instead of the least symptomatic limb, and therefore may be more easily detected. At one-year follow-up, we found a meaningful improvement in plantar flexor endurance of the injured limb in both groups, which exceeded the smallest detectable change (i.e. 3.7 repetitions),[41] and to a level superior to that of the non-injured limb. We did not find a significant difference between the programmes, although improvement in the AG was greater (2.7, 95% CI [-0.5, 5.9], $P = 0.092$). This may indicate that the Alfredson programme is more effective in restoring muscular endurance of the plantar flexors than the Silbernagel programme, but this could not be supported with previous research on these loading programmes due to discrepancy in outcome measures. A possible explanation could be that eccentric contractions result in greater improvement of muscle strength and mass than concentric contractions due to the higher loads developed during eccentric loading.[42] However, since we did not monitor the exact training load in our participants, it is unknown whether this explanation applies to the trend seen in our data. Another possible explanation may be that the AG exercised twice per day instead of once daily as was performed by the SG. Nonetheless, the underpowered nature of our study affects the precision of our estimates, and impedes from drawing a firm conclusion on possible dis-

crepancy in improvement of plantar flexor endurance between both groups. This should be subject of future adequately powered research.

By adding the CMJ, we aimed to investigate the reactive strength of the plantar flexor muscle-tendon complex. In contrast to the heel-raise test, we were not able to determine a significant improvement of jump height, neither within nor between the groups. In other studies, improvement on the CMJ after following the Silbernagel programme was found in some,[22] but not all patients.[21]
The responsiveness to change of the CMJ is thought to be limited.[32] This may be explained by the inability of CMJ to isolate plantar flexor muscle-tendon function,[6] as it also requires considerable activity and coordination of muscle groups of the upper leg and hip.[43] Hence, performance of other (proximal) muscle groups may compensate for the diminished function of the plantar flexor muscle-tendon complex. Furthermore, although the last phase of the Silbernagel programme incorporated quick-rebounding and plyometric exercises, most exercises from both programmes encompassed low-velocity heel-raises. It is likely that these low-velocity movements have limited translation into improved high-velocity movements such as the CMJ, which may explain why we could not detect a significant improvement of jump height.

Our findings showed improvement of hip muscle strength from baseline to one-year follow-up in both groups, but only for the external rotators this improvement was significant. We previously found weakness in the hip abductors, extensors and external rotators in patients with midportion AT, but in this cross-sectional study data were not longitudinally assessed.[8] To our knowledge, only Sancho et al. performed a longitudinal assessment of hip muscle strength in AT.[44] They showed improved hip abduction strength after following a progressive exercise programme including isometric and isotonic exercises, and a hopping programme including double-leg and single-leg hops. It is reasonable to suggest that addition of hopping exercises addresses hip muscle function to a greater extent than solely heel-raising exercises as performed in our study. Therefore, improvement of hip strength in the current study presumably is the result of increased activity level during the study, rather than a specific effect of the loading programmes. For future studies, it would be interesting to prospectively investigate the role of hip muscle strength in relation to AT.

Returning to previous sports level is the ultimate goal of rehabilitation and an important milestone for many patients.[45] Yet, RTS is not regularly included as an outcome measure in intervention trials.[34] We found a considerably higher RTS rate in the SG than in the AG (i.e. 68% vs. 38%), but this difference appeared not significant, most probably due to the small sample size increasing the chance of a type II error. The imbalance in sport types between the groups at baseline may also have affected the RTS rate. Yet, we still feel this is an interesting finding. It may indicate that patients in the SG were better prepared for RTS than patients in the AG, possibly because the Silbernagel programme comprises a combination of different contraction modes, including quick-rebounding and plyometric exercises.

However, further adequately powered research is warranted to validate our findings and further explore potential explanatory mechanisms.

Strengths and limitations
We designed our study considering key methodological issues, such as randomisation, concealment of allocation and intention-to-treat analysis, to minimize potential risk of bias. Furthermore, by minimizing the supervising sessions, we incorporated an intervention that is inexpensive to implement in clinical practice.
The underpowered sample size is an important limitation of our study. Unforeseen, we struggled to enroll sufficient participants. The outbreak of COVID-19 caused additional difficulties. Consequently, we decided to terminate recruitment of participants before having reached the intended sample size. To accelerate inclusion, we frequently contacted the potential referrers to remind them of our study, but it did not result in more participants. The limited sample size increases the chance of a type I or II error, and therefore, we emphasize that conclusions should be interpreted with caution.

CONCLUSION

We found that both the Alfredson and the Silbernagel loading programme yield improvement in functional performance of the lower extremity in recreational athletes with AT. Our findings show meaningful improvement of plantar flexor muscular endurance up to one year follow-up, with a trend towards greater improvement in favor of the Alfredson programme. We also found a marked improvement in hip external rotator strength in both groups up to one-year follow-up, but not in jump height, and strength of the hip extensors and abductors. No significant differences between both programmes were found for jump height and hip muscle strength. At one-year follow-up, the Silbernagel programme was associated with a more than 80% better RTS rate than de Alfredson programme.

REFERENCES

1. Francis P, Whatman C, Sheerin K, et al. The proportion of lower limb running injuries by gender, anatomical location and specific pathology: a systematic review. *J Sports Sci Med* 2019;18(1):21-31.
2. Chang YJ, Kulig K. The neuromechanical adaptations to Achilles tendinosis. *J Physiol* 2015;593(15): 3373-87.
3. Sancho I, Malliaras P, Barton C, et al. Biomechanical alterations in individuals with Achilles tendinopathy during running and hopping: A systematic review with meta-analysis. *Gait Posture* 2019;73:189-201.
4. Hein T, Janssen P, Wagner-Fritz U, et al. Prospective analysis of intrinsic and extrinsic risk factors on the development of Achilles tendon pain in runners. *Scand J Med Sci Sports* 2014;24(3):e201-e12.
5. Mahieu N, Witvrouw E, Stevens V, et al. Intrinsic risk factors for the development of achilles tendon overuse injury: a prospective study. *Am J Sports Med* 2006;34(2):226-35.
6. McAuliffe S, Tabuena A, McCreesh K, et al. Altered strength profile in Achilles tendinopathy: a systematic review and meta-analysis. *J Athl Train* 2019;54(8):889-900.
7. Wyndow N, Cowan SM, Wrigley TV, et al. Triceps surae activation is altered in male runners with Achilles tendinopathy. *J Electromyogr Kinesiol* 2013;23(1):166-72.
8. Habets B, Smits HW, Backx FJG, et al. Hip muscle strength is decreased in middle-aged recreational male athletes with midportion Achilles tendinopathy: a cross-sectional study. *Phys Ther Sport* 2016;25:55-61.
9. Franettovich Smith MM, Honeywill C, Wyndow N, et al. Neuromotor control of gluteal muscles in runners with achilles tendinopathy. *Med Sci Sports Exerc* 2014;46(3):594-99.
10. Honeywill C, Creaby M, Smith M, et al. Altered neuromotor control of the Gluteus medius and Gluteus maximus in male runners with Achilles tendinopathy. *J Sci Med Sport* 2012;15:S64-S65.
11. Debenham JR, Travers MJ, Gibson W, et al. Achilles tendinopathy alters stretch shortening cycle behaviour during a sub-maximal hopping task. *J Sci Med Sport* 2016;19(1):69-73.
12. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.
13. Sussmilch Leitch SP, Collins NJ, Bialocerkowski AE, et al. Physical therapies for Achilles tendinopathy: systematic review and meta-analysis. *J Foot Ankle Res* 2012;5(1):15.
14. Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: A systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.
15. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.
16. Martin RL, Chimenti R, Cuddeford T, et al. Achilles pain, stiffness, and muscle power deficits: Midportion Achilles tendinopathy revision 2018. *J Orthop Sports Phys Ther* 2018;48(5):A1-A38.
17. Silbernagel KG, Thomeé R, Eriksson BI, et al. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med* 2007;41(4):276-80.
18. Yu JH, Park DS, Lee GC. Effect of eccentric strengthening on pain, muscle strength, endurance, and functional fitness factors in male patients with Achilles tendinopathy. *Am J Phys Med Rehabil* 2013;92(1):68-76.
19. Habets B, van Cingel REH, Backx FJG, et al. Alfredson versus Silbernagel exercise therapy in chronic midportion Achilles tendinopathy: study protocol for a randomized controlled trial. *BMC Musculoskelet Disord* 2017;18(1):296.
20. Alfredson H, Pietilä T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26(3):360-66.
21. Silbernagel KG, Thomeé R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35(6):897-906.
22. Silbernagel KG, Thomee R, Thomee P, et al. Eccentric overload training for patients with chronic Achilles tendon pain--a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports* 2001;11(4):197-206.
23. Hutchison AM, Evans R, Bodger O, et al. What is the best clinical test for Achilles tendinopathy? *Foot Ankle Surg* 2013;19(2):112-17.
24. Reiman M, Burgi C, Strube E, et al. The utility of clinical measures for the diagnosis of Achilles tendon injuries: a systematic review with meta-analysis. *J Athl Train* 2014;49(6):820-29.
25. Gaida JE, Alfredson H, Kiss ZS, et al. Asymptomatic Achilles tendon pathology is associated with a central fat distribution in men and a peripheral fat distribution in women: a cross sectional study of 298 individuals. *BMC Musculoskelet Disord* 2010;11:41.
26. Konor MM, Morton S, Eckerson JM, et al. Reliability of three measures of ankle dorsiflexion range of motion. *Int J Sports Phys Ther* 2012;7(3):279-87.
27. Allen RH, Gross MT. Toe flexors strength and passive extension range of motion of the first metatarsophalangeal joint in individuals with plantar fasciitis. *J Orthop Sports Phys Ther* 2003;33(8):468-78.
28. Moller M, Lind K, Styf J, et al. The reliability of isokinetic testing of the ankle joint and a heel-raise test for endurance. *Knee Surg Sports Traumatol Arthrosc* 2005;13(1):60-71.
29. Macdermid JC, Silbernagel KG. Outcome evaluation in tendinopathy: foundations of assessment and a summary of selected measures. *J Orthop Sports Phys Ther* 2015;45(11):950-64.
30. Lunsford BR, Perry J. The standing heel-rise test for ankle plantar flexion: criterion for normal. *Phys Ther* 1995;75(8):694-98.
31. Markovic G, Dizdar D, Jukic I, et al. Reliability and factorial validity of squat and countermovement jump tests. *J Strength Cond Res* 2004;18(3):551-5.

32. Silbernagel KG, Gustavsson A, Thomeé R, et al. Evaluation of lower leg function in patients with Achilles tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2006;14(11):1207-17.

33. Thorborg K, Petersen J, Magnusson SP, et al. Clinical assessment of hip strength using a hand-held dynamometer is reliable. *Scand J Med Sci Sports* 2010;20(3):493-501.

34. Habets B, van den Broek AG, Huisstede BMA, et al. Return to sport in athletes with midportion Achilles tendinopathy: a qualitative systematic review regarding definitions and criteria. *Sports Med* 2017;48(3):705-23.

35. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2012;10(1):28-55.

36. Fitzmaurice GM, Laird NM, Ware J. Applied longitudinal analysis. New York: John Wiley and Sons 2012.

37. Lemmer JT, Hurlbut DE, Martel GF, et al. Age and gender responses to strength training and detraining. *Med Sci Sports Exerc* 2000;32(8):1505-12.

38. Knobloch K, Schreibmueller L, Kraemer R, et al. Gender and eccentric training in Achilles mid-portion tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2010;18(5):648-55.

39. Alfredson H, Nordstrom P, Pietila T, et al. Bone mass in the calcaneus after heavy loaded eccentric calf-muscle training in recreational athletes with chronic achilles tendinosis. *Calcif Tissue Int* 1999;64(5):450-55.

40. Murphy M, Rio E, Debenham J, et al. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: a review of outcome measures for self- reported pain and function. *Int J Sports Phys Ther* 2018;13(2):283-92.

41. Segura-Orti E, Martinez-Olmos FJ. Test-retest reliability and minimal detectable change scores for sit-to-stand-to-sit tests, the six-minute walk test, the one-leg heel-rise test, and handgrip strength in people undergoing hemodialysis. *Phys Ther* 2011;91(8):1244-52.

42. Roig M, O'Brien K, Kirk G, et al. The effects of eccentric versus concentric resistance training on muscle strength and mass in healthy adults: a systematic review with meta-analysis. *Br J Sports Med* 2009;43(8):556-68.

43. Mackala K, Stodolka J, Siemienski A, et al. Biomechanical analysis of squat jump and countermovement jump from varying starting positions. *J Strength Cond Res* 2013;27(10):2650-61.

44. Sancho I, Morrissey D, Willy RW, et al. Education and exercise supplemented by a pain-guided hopping intervention for male recreational runners with midportion Achilles tendinopathy: A single cohort feasibility study. *Phys Ther Sport* 2019;40:107-16.

45. Silbernagel KG, Crossley KM. A proposed return-to-sport program for patients with midportion Achilles tendinopathy: Rationale and implementation. *J Orthop Sports Phys Ther* 2015;45(11):876-86.

CHAPTER 6

Hip muscle strength is decreased in middle-aged recreational male athletes with midportion Achilles tendinopathy: a cross-sectional study

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ABSTRACT

Objective: Investigating differences in hip muscle strength between athletes with Achilles tendinopathy (AT) and asymptomatic controls.

Design: Cross-sectional case-control study.

Setting: Sports medical center.

Participants: Twelve recreational male athletes with mid-portion AT and twelve matched asymptomatic controls.

Outcome measures: Isometric strength of the hip abductors, external rotators, and extensors was measured using a handheld dynamometer. Functional hip muscle performance was evaluated with the single-leg squat. The Victorian Institute of Sport Assessment–Achilles (VISA-A) questionnaire was completed to determine clinical severity of symptoms.

Results: Compared to controls, participants with AT demonstrated 28.9% less isometric hip abduction strength ($P = 0.012$), 34.2% less hip external rotation strength ($P = 0.010$), and 28.3% less hip extension strength ($P = 0.034$) in the injured limb. Similar differences were found for the non-injured limb (26.7-41.8%; $P < 0.03$). No significant differences were found in functional hip muscle performance between the injured and non-injured limb or between the groups, and no significant correlation was found between hip muscle strength and VISA-A scores.

Conclusion: Recreational male athletes with chronic mid-portion AT demonstrated bilateral weakness of hip abductors, external rotators, and extensors compared to their asymptomatic counterparts. These findings suggest that hip muscle strength may be important in the assessment and rehabilitation of those with AT.

INTRODUCTION

Achilles tendinopathy (AT) is a clinical syndrome of the Achilles tendon, characterized by activity-related pain, swelling, and impaired performance.[1 2] Most ATs are localized in the mid-portion of the tendon.[2 3] Incidence of the injury is highest in sports that involve running and jumping, with the highest prevalence reported in middle-aged men.[4 5] Management of AT can be difficult,[6 7] and the injury may cause long-term limitations in sports participation.

Conservative treatment is considered the primary choice, mostly for a period of 3-6 months.[3 8 9] Within this period eccentric calf muscle loading is the most effective treatment strategy.[9-11] However, it has been stated that in a considerable proportion of patients with AT, eccentric loading is not successful and symptoms and impairments persist.[12 13]

There are multiple reasons why eccentric loading may not be successful. Various etiological factors, such as age, foot type, decreased lower extremity flexibility, and (excessive) training load can play a role.[14-16] It may also be that strengthening of the calf muscle-tendon unit alone does not adequately restore lower limb performance, indicating that rehabilitation of AT should also focus on restoring the function of the proximal kinetic chain.[3 17 18] This kinetic chain is described as a system of multiple body segments that move in a coordinated and sequential manner to optimize position and velocity of the distal segment.[19] Optimal functioning of the kinetic chain is affected by alterations in joint kinematics, muscular balance and neuromuscular control. In this functioning, proximal muscle strength is considered to be essential.[19] Therefore, dysfunction of the proximal muscle groups of the kinetic chain (e.g. hip musculature) could be associated with excessive loading of the distal parts (e.g. Achilles tendon) during sport activities. However, empirical evidence for this hypothesis is lacking.

There is growing evidence that decreased hip muscle strength is associated with several lower extremity injuries. For example, patients with patellofemoral pain syndrome,[20-22] and posterior tibial tendon dysfunction[23] demonstrate decreased isometric hip muscle strength compared to non-injured subjects. Decreased strength of the hip abductors and external rotators may cause increased femoral adduction and internal rotation and, consequently, lead to excessive knee valgus angles.[24] These pathomechanics could potentially replace the line of weight bearing on the medial side of the subtalar joint,[24] resulting in a whipping action of the Achilles tendon due to altered gastrocnemius length and excessive foot pronation.[25 26] Also, strength deficits of the hip extensors may cause increased compensatory m. triceps surae activity during the landing and push off phase in running.[27] In summary, diminished strength of the relatively strong proximal hip muscle groups may lead to increased Achilles tendon stress and this may be linked to mid-portion AT. To our knowledge, a possible association between decreased hip muscle strength and mid-portion AT has not yet been investigated. Therefore, the primary objective of this study was to

investigate differences in hip muscle strength between athletes with chronic mid-portion AT and matched asymptomatic controls. Secondary aims were to investigate: 1) differences in functional performance of the hip muscle groups during the single leg squat, 2) differences in hip muscle strength and functional performance between the injured and non-injured limb, and 3) the association between hip muscle strength and clinical severity of symptoms of AT. It was hypothesized that participants with mid-portion AT would demonstrate decreased strength and functional performance of the hip musculature in their injured limb compared to asymptomatic controls and their uninjured limb, and that these strength deficits would be positively associated with the severity of their symptoms.

MATERIALS AND METHODS

Study design

A cross-sectional case-control study with two groups was conducted. One group consisted of recreational male athletes with chronic mid-portion AT (AT group), while the other consisted of matched asymptomatic controls (control group). Matching was based on age (± 5 years), sport type, and current training extent categorized in three groups (i.e. < 3 h/week, 3-7 h/week, and > 7 h/week). Written informed consent was obtained prior to participation. The study protocol was approved by the institutional review board of the University Medical Center Utrecht (registration number 14-112).

Study population

Recreational male athletes with chronic mid-portion AT were recruited between February and June 2014. Primarily, participants were recruited through direct referrals from sports physicians at Papendal Sports Medical Center, Arnhem, The Netherlands, and general practitioners in the surrounding region. Additionally, recruitment was performed through mailings and advertisements at local sport clubs. Controls were recruited through e-mail/personal contact with employees at the National Sports Center Papendal, Arnhem, The Netherlands and the University Medical Center Utrecht, Utrecht, The Netherlands, and local sports clubs.

Potential participants were initially contacted by telephone by the principal investigator (PI), in order to determine their eligibility. Participants were eligible for inclusion if they were males aged 21-60 years,[4] and if they were practicing a sport involving running and/or jumping. Potential participants were excluded if they had a diagnosis of insertional AT, bilateral mid-portion AT, a history of Achilles tendon rupture, if they had a corticosteroid injection in the Achilles tendon in the previous 12 months, other injuries of the lower extremity during the past 12 months, or if they had a neurological or systemic disease. If a participant was eligible for inclusion, an appointment was made for physical examination at a physiotherapy department. The AT group had a clinical diagnosis of unilateral mid-portion AT (diagnosed by a physician or physiotherapist),[2] with a duration of symptoms of ≥ 3 months. Diagnosis of mid-portion AT was confirmed by the PI using two clinical signs: 1) subjective self-reported activity-related pain at 2-6 cm proximal to the calcaneal insertion, 2) pain on palpation by the examiner. Interrater reliability of these signs is shown to be good (κ = 0.746 and 0.738 respectively),[28] and these signs were also used in the control group to rule out AT. Subsequently, all measurements were performed by the PI, who was not blinded to group status (i.e. AT or control group).

Outcome measures

Characteristics of the participants were collected, including age, height, and body weight. Additionally, we collected several variables considered important in the kinetic chain, that may also be associated with mid-portion AT. Potential differences in these variables between the groups may introduce bias in the interpretation of the results. Ankle dorsiflexion range of motion (ROM) was measured with the weight-bearing lunge test,[29] and extension ROM of the first metatarsophalangeal joint (MTP-1) was measured with a standard goniometer.[30] Hip joint ROM values related to takeoff were recorded for extension and internal rotation with a goniometer.[31 32] Finally, duration of symptoms (months) and treatment (yes/no) were collected for the AT group, and use of (pain) medication (yes/no) was recorded for both groups.

All measurements were performed for the injured limb in the AT group, and for the corresponding limb of the control group. The non-injured limb of participants in the AT group was also measured for comparison between the injured and non-injured side.

Isometric strength

Isometric strength was measured with a Microfet 2 hand-held dynamometer (HHD). Thorborg and colleagues[33] have shown that this is a reliable method for measuring hip muscle strength, with intraclass correlation coefficients ranging from 0.74-0.95 and standard error of measurement values ranging from 4-11%. For all measurements, participants were asked to give a maximal isometric effort in the test direction (i.e. abduction, external rotation, and extension), and hold for this 5 s (make method), without providing verbal encouragement. Before the actual test, participants performed two submaximal trial repetitions. Subsequently, three test repetitions were performed, separated by 30 s of recovery.[33] The best repetition was used for the data analysis.

Hip abduction strength was measured with the participant in side-lying position on an examination table.[34] The contralateral leg was flexed ± 30° at the hip and knee, to enhance stability and comfort. The test leg was placed in 0° of hip flexion and 10° of hip abduction with the knee fully extended. A strap was placed over the iliac crest and attached to the underside of the table. The HHD was placed on the lateral side of the femur, 5 cm proximal to the lateral femoral condyle; it was secured by a second strap, which was also attached to the underside of the table.

For strength testing of the external rotators, participants sat on an examination table with the hips and knees flexed to 90° and the feet off the ground.[21] A strap was used for stabilization of the ipsilateral thigh, and participants placed their arms behind their back. The HHD was placed 5 cm proximal to the medial malleolus and was secured by a strap that was fixed on the table base.

Hip extensors strength was measured with the participant lying prone on an examination table, with the hip in neutral position and the knee flexed to 90°.[33] A strap was placed at the height of the iliac crest to stabilize the pelvis. The HHD was placed 5 cm proximal to the popliteal fossa at the posterior thigh.

Functional performance

As isometric strength measurements only provide insight into isolated muscle function, we also included a measure of functional performance of the hip musculature using the single-leg squat. This has been shown a reliable method to identify hip muscle dysfunction.[35] The test was performed as described by Crossley et al.[35] Participants were measured barefoot and in their underwear. They were asked to stand on one leg on a 20-cm box, with their arms folded across their chest. Then they had to perform a squat until 60° of knee flexion was achieved and then push themselves up again. Squats were performed at a rate of approximately one squat per 2 s, and the depth of the squat was determined with a goniometer. Prior to the actual test, the procedure and technique were demonstrated by the investigator and participants were allowed three trial repetitions. The actual test was performed directly after practicing and comprised five consecutive test repetitions. These test repetitions were recorded with a video camera, placed about 2 m in front of the participant at the height of the participant's pelvis. Video recordings were stored in a coded manner and used for data analysis (i.e. rating of performance).

Rating was performed by the PI using a three-point ordinal scale ("good", "fair", and "poor") as recommended by Crossley et al.[35] The rating criteria (with the respective requirements to fulfill a criterion) were:

- overall impression for the five trials (maintaining balance, perturbations, depth and speed);
- posture of the trunk over the pelvis (trunk/thoracic lateral deviation or shift, rotation, lateral flexion, forward flexion);
- posture of the pelvis (pelvic shunt or lateral deviation, rotation, pelvic tilt);
- hip joint posture and movement (hip adduction, femoral internal rotation);
- knee joint posture and movement (apparent knee valgus, knee position relative to foot position).

A criterion was satisfied if all requirements for that criterion were met. The performance of the single-leg squat was rated as "poor" if a participant did not fulfill at least one criterion for all test repetitions (i.e. not all requirements for any of the criteria were met). If a participant met all requirements for one, two, or three criteria for all test repetitions, the performance was rated as "fair". The performance on the single-leg squat was rated as "good" when a participant satisfied all requirements for at least 4 out of 5 criteria for all test repetitions.

Clinical severity of symptoms

Clinical severity of AT was measured with the Victorian Institute for Sport Assessment–Achilles (VISA-A) questionnaire, which is a valid and reliable tool covering the domains of pain, functioning in daily activity, and sports activity.[36] Scores range from 0 to 100, with 100 indicating a perfect asymptomatic score. The VISA-A score was used to investigate the association between hip muscle strength and clinical severity of symptoms.

Data analysis

Sample size was calculated using G*Power 3.1.5,[37] assuming 1-β = 0.80 and α (two-sided) = 0.05. A strength difference of the hip muscles of 28.4-33.8% has been reported in patients with posterior tibial tendon dysfunction compared to matched asymptomatic controls.[23] Assuming a strength difference of 28.4%, a minimum of 12 participants per group was required.

Data verification was performed by a research assistant who only had access to the encrypted data. After data input was verified, normality of the data was checked visually with Q-Q plots and statistically using the Shapiro-Wilk test. As data were not normally distributed, non-parametric tests were used. Descriptive statistics were calculated for demographic and anthropometric variables, and differences between groups and between the injured and non-injured limb were investigated using the Wilcoxon signed rank test.

Before further analysis, peak isometric strength measures were corrected for body weight.[21] The Wilcoxon signed rank test was used to compare isometric strength of the hip abductors, external rotators, and extensors between the AT and control group, and for comparison between the injured and non-injured limb among participants in the AT group. Differences in functional performance, as measured with the single-leg squat, were investigated with the McNemar-Bowker test. Spearman's rank correlation coefficients were used to investigate the association between isometric strength and VISA-A scores. Statistical significance was set at α = 0.05.

RESULTS

Participants

A total of 24 participants (12 in each group) were included (median age AT group = 51.5 years, interquartile range [IQR] 43-53; median age control group = 49.5 years, IQR 42-53.5). There were no significant differences in demographic and anthropometric characteristics between the groups, or between the injured and non-injured limb of the AT group (Table 6.1, $P > 0.05$). The AT group had a median duration of symptoms of approximately 18 months (IQR 9.3-50.8), and the median VISA-A score was 63 (IQR 50-78.8). Seven participants in the AT group had received (conservative) treatment for their injury. None of the participants used (pain) medication at the time of the study.

Isometric strength

The AT group showed significantly less isometric strength in their hip abductors, external rotators, and extensors compared with the control group (Table 6.2, $P < 0.035$). The highest between-group difference for the injured limb was found for external rotation (34.2%, $P = 0.010$), whereas the differences for hip abduction and extension were smaller (28.9%, $P = 0.012$, and 28.3%, $P = 0.034$, respectively). Strength differences for the non-injured limb compared to the control group were 41.8% ($P = 0.003$) for the external rotators, 30.5% ($P = 0.010$) for the abductors, and 26.7% ($P = 0.023$) for the hip extensors. No significant differences were found in isometric strength between the injured and non-injured limb in the AT group.

Table 6.1 Demographic and anthropometric characteristics of the study population

	AT group: injured side (n=12)	AT group: non-injured side (n=12)	*P*-value[a]	Control group (n=12)	*P*-value[b]
Age (years)[c]	51.5 (43.0-53.0)			49.5 (42.0-53.5)	0.529
Height (cm)[c]	189.0 (181.3-192.0)			181.5 (179.3-185.8)	0.082
Weight (kg)[c]	80.5 (75.0-92.9)			80.5 (69.5-88.9)	0.136
BMI (kg/m^2)[c]	22.7 (21.8-26.8)			23.7 (21.7-26.2)	0.754
Sport type (N)					
- Running	9			9	
- Soccer	1			1	
- Volleyball	1			1	
- Tennis	1			1	
Training extent (N)					
- < 3 hours/week	4			4	
- 3-7 hours/week	7			7	
- > 7 hours/week	1			1	
Sports experience (years)[c]	34.0 (22.5-39.3)			40.0 (22.5-42.3)	0.624
Weight-bearing lunge test (cm)[c]	11.3 (8.9-14.5)	11.5 (10.5-14.1)	0.959	13.3 (9.0-14.4)	0.969
MTP-1 extension ROM (°)[c]	49.0 (21.8-60.0)	43.0 (21.0-62.0)	0.283	53.0 (44.0-57.0)	0.582
Hip extension ROM (°)[c]	17.0 (10.5-21.8)	16.0 (14.0-23.0)	0.473	17.5 (14.0-22.0)	0.372
Hip internal rotation ROM (°)[c]	23.0 (15.0-30.0)	28.0 (18.5-35.8)	0.050	22.0 (20.0-28.8)	0.799
Injured side (left/right) (N)	4/8				
Duration of symptoms (months)[c]	17.5 (9.3-50.8)				
VISA-A score[c]	63.0 (50.0-78.8)				
Current treatment (yes/no) (N)	7/5				
Use of pain medication (yes/no) (N)	0/12			0/12	

AT= Achilles tendinopathy; *ROM* = range of motion; *MTP-1* = first metatarsophalangeal joint; *VISA-A* = Victorian Institute of Sport Assessment – Achilles

[a] *P*-values for differences between the injured and non-injured limb

[b] *P*-values for differences between the AT group and control group

[c] Data are reported as median (lower bound – upper bound interquartile range)

Functional performance

Functional performance, evaluated with the single-leg squat, showed no significant difference between or within the two groups (Table 6.3, $P > 0.05$ for all comparisons).

Association between isometric strength and clinical severity

No significant correlation was found for any of the isometric strength measurements and the VISA-A score, with ρ=0.25, ρ=0.21, and ρ=0.06 for abduction, external rotation, and extension, respectively ($P > 0.4$).

Table 6.2 Isometric strength values of hip abductors, external rotators, and extensors for participants in the Achilles tendinopathy group and control group

	AT group: injured side (n = 12)		AT group: non-injured side (n = 12)			Control group (n = 12)		
	Strength values (N)	**% BW (N/kg)**	**Strength values (N)**	**% BW (N/kg)**	***P*-value[a]**	**Strength values (N)**	**% BW (N/kg)**	***P*-value[b]**
Hip abduction[c]	245.1 (182.3-289.7)	2.66 (2.29-3.11)	244.0 (184.7-288.9)	2.60 (2.31-3.12)	0.875	298.4 (258.3-374.2)	3.74 (3.29-5.03)	0.012[d]
Hip external rotation[c]	117.6 (76.0-126.6)	1.29 (0.86-1.55)	109.6 (79.9-127.1)	1.14 (0.79-1.68)	0.754	136.3 (129.5-190.7)	1.96 (1.56-2.20)	0.010[d]
Hip extension[c]	127.7 (84.6-160.5)	1.37 (1.05-1.83)	133.2 (87.4-153.8)	1.41 (1.05-1.75)	0.814	156.6 (124.7-207.6)	1.91 (1.51-2.45)	0.034[d]

AT = Achilles tendinopathy; *BW* = body weight
[a] *P*-values for differences in % BW between the injured and non-injured limb
[b] *P*-values for differences in % BW between the AT group and control group
[c] Data are reported as median (lower bound – upper bound interquartile range)
[d] Significant difference at the 0.05 level

Table 6.3 Performance on the single-leg squat for participants in the Achilles tendinopathy group and the control group

	AT group: injured side (n = 12)	AT group: non-injured side (n = 12)	***P*-value[a]**	Control group (n = 12)	***P*-value[b]**
Good[c] (n)	0	0	0.180	2	0.350
Fair[c] (n)	4	7		6	
Poor[c] (n)	8	5		4	

AT = Achilles tendinopathy
[a] *P*-value for difference between the injured and the non-injured limb (McNemar-Bowker test)
[b] *P*-value for difference between the AT group injured limb and the control group (McNemar-Bowker test)
[c] Rating was performed according to Crossley et al.[35]

DISCUSSION

To the best of our knowledge, this is the first study to investigate hip muscle strength in male athletes with AT compared with controls. Our results show that recreational male athletes with chronic mid-portion AT have significantly less isometric strength in the hip abductors, external rotators, and extensors of their injured and non-injured limb compared to their asymptomatic counterparts. When corrected for body weight, these differences ranged from 26.7-41.8%, which is considerably larger than the measurement error found for isometric strength measures using a HHD (i.e. 4-11%).[33] We think that this bilateral weakness is an interesting finding, which may be a result of an average of 18 months of inactivity or involvement of the central nervous system. The latter is in agreement with a recent systematic review showing that motor deficits can present bilaterally in unilateral lateral epicondylalgia,[38] although it should be noted that motor deficits in AT may differ from upper limb tendinopathy, as Achilles tendon loading often involves energy storage and release in (bilateral) weight-bearing activities, compared to (unilateral) non weight-bearing activities for many upper limb tendons.

The strength values that were found in the control group are comparable to hip muscle strength values found in a different study that investigated 253 healthy men with an average age of 49 years.[39] Hence, if the strength values found in the AT group of our study are compared to these normative values, differences seem to be quite similar, which may strengthen our findings of decreased hip muscle strength in a population of recreational males with AT. However, as measurement positions differ, this conclusion should be made with caution.

Decreased hip muscle strength found in the AT group is in keeping with findings of previous studies, in which decreased and delayed electromyographic activity of the gluteus medius[40] and maximus[41] was demonstrated in athletes with AT, indicating altered neuromotor control of the hip musculature. Our study demonstrates decreased isometric hip muscle strength in patients with AT, which (together with appropriate neuromotor control) is considered essential for proper kinetic chain function.[19] However, isometric strength measurements only provide insight into isolated hip muscle function, which differs from sport-specific movements. Therefore, we also included a measure of functional performance, i.e. the single-leg squat. In this way, we attempted to challenge the neuromotor control of the hip musculature. Our results reveal no significant differences in performance on the single-leg squat between the two groups (or between injured/uninjured limb). However, whilst this test is recommended as a measure of hip muscle function,[35] the single-leg squat also assesses strength and coordination of other muscle groups of the lower extremity and trunk. Additionally, it was interesting that only two out of 12 participants in the control group were rated as 'good', which questions the use of the single-leg squat as a functional measure of hip muscle function in our study population.

The use of video analysis during rating according to the criteria of Crossley et al.[35] may also be a subject of debate, as this only provides a two-dimensional and subjective manner of functional hip muscle assessment. Additional resources, such as reflective markers or electromyographic measurements, might have objectified the rating of functional hip muscle performance during single-leg squat. It may be that these more objective rating methods would have revealed a difference in functional performance between the groups.

Our results are also consistent with findings in patients with patellofemoral pain syndrome and posterior tibial tendon dysfunction, in which isometric strength differences of the hip musculature of 21-36% were reported.[20 21 23] These strength deficits are associated with altered lower extremity kinematics such as increased femoral adduction and internal rotation and, consequently, excessive pronation of the foot.[42] These pathomechanics are frequently proposed as a cause of several lower extremity injuries,[42] but studies investigating lower extremity kinematics in relation to AT are scarce. Kulig et al.[43] retrospectively investigated the take-off phase of the saut de chat in dancers with a history of AT, and found significantly greater peak hip adduction and internal rotation angles compared with healthy controls. Additionally, a study in runners demonstrated that subjects with a history of AT showed a relatively increased internal rotation of the femur compared to subjects with no history of AT.[44] It was suggested that this internal rotation may alter gastrocnemius length and thereby increase stress on the Achilles tendon. Decreased strength of the hip musculature, as demonstrated in the present study, may contribute to altered lower limb biomechanics and, consequently, may be associated with AT. Hip muscle strengthening may therefore be of added value in the management of patients with chronic AT, but this cannot be concluded from our study and is an area of future investigation.

Besides differences in hip muscle strength between athletes with AT and asymptomatic controls, this study also aimed to investigate the correlation between strength and the severity of symptoms. Our results showed no significant correlation, indicating that the isometric strength differences found are not necessarily associated with the severity of the injury. However, because our sample size calculation was based on the primary study aim, our relatively small sample does not provide sufficient power to accurately prove this association. The small sample size also precluded us from assessing the relationship between isometric hip muscle strength and hip muscle performance, which would be an interesting topic for future research.

A strength of this study is that the two groups were matched on age, sport type, and training extent, which are important factors that may introduce strength differences.[45] The study also has some limitations. First, the cross-sectional design makes it impossible to determine whether the strength differences found are a cause or a consequence of the injury. The athletes with AT had a median duration of symptoms of 18 months, and therefore, the strength differences observed might also be a result of disuse and altered motor patterns rather than a cause of the injury.[21] The fact that bilateral weakness was present compared with the asymptomatic controls, further questions a causal relationship and might imply a compensatory motor deficit through central nervous system involvement.[38] Prospective research is needed to determine the exact relationship between hip muscle weakness and mid-portion AT. A second limitation concerns the fact that the investigator was not blinded to group status during the examination. However, for the isometric strength measurements, the examinator's influence was minimized by using external straps for fixation of the HHD and providing no verbal encouragement. For the rating of the single-leg squat the non-blinding may have affected the rating, but since no between-group difference was found, possible bias seems to be limited.

CONCLUSION

This study shows that recreational middle-aged male athletes with chronic mid-portion AT demonstrate significant weakness in the hip abductors, external rotators, and extensors of both limbs compared to matched asymptomatic controls. No difference was found in functional hip performance between the two groups. Due to the cross-sectional design of this study, it is unknown whether the strength differences are a cause or a consequence of the injury, or a combination. Prospective research is needed to determine this relationship. Based on our findings, clinicians may consider hip muscle strength in the assessment and rehabilitation of middle-aged recreational male athletes with chronic mid-portion AT.

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REFERENCES

1. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. *Arthroscopy* 1998;14(8):840-43.

2. van Dijk CN, van Sterkenburg MN, Wiegerinck JI, et al. Terminology for Achilles tendon related disorders. *Knee Surg Sports Traumatol Arthrosc* 2011;19(5):835-41.

3. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: new treatment options. *Br J Sports Med* 2007;41(4):211-16.

4. De Jonge S, Van den Berg C, De Vos RJ, et al. Incidence of midportion Achilles tendinopathy in the general population. *Br J Sports Med* 2011;45(13):1026-28.

5. Satyendra L, Byl N. Effectiveness of physical therapy for Achilles tendinopathy: an evidence based review of eccentric exercises. *Isokinet Exerc Sci* 2006;14(1):71-80.

6. Alfredson H. Chronic midportion Achilles tendinopathy: an update on research and treatment. *Clin Sports Med* 2003;22(4):727-41.

7. Cook J, Purdam CR. The challenge of managing tendinopathy in competing athletes. *Br J Sports Med* 2014;48(7):506-09.

8. Rompe J, Furia J, Maffulli N. Mid-portion Achilles tendinopathy -- current options for treatment. *Disabil Rehabil* 2008;30(20-22):1666-76.

9. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.

10. Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: A systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.

11. Sussmilch Leitch SP, Collins NJ, Bialocerkowski AE, et al. Physical therapies for Achilles tendinopathy: systematic review and meta-analysis. *J Foot Ankle Res* 2012;5(1):15.

12. Maffulli N, Walley G, Sayana MK, et al. Eccentric calf muscle training in athletic patients with Achilles tendinopathy. *Disabil Rehabil* 2008;30(20-22):1677-84.

13. Ram R, Meeuwisse W, Patel C, et al. The limited effectiveness of a home-based eccentric training for treatment of Achilles tendinopathy. *Clin Invest Med* 2013;36(4):E197-206.

14. Jarvinen TA, Kannus P, Maffulli N, et al. Achilles tendon disorders: etiology and epidemiology. *Foot Ankle Clin* 2005;10(2):255-66.

15. Kaufman KR, Brodine SK, Shaffer RA, et al. The effect of foot structure and range of motion on musculoskeletal overuse injuries. *Am J Sports Med* 1999;27(5):585-93.

16. Paavola M, Kannus P, Järvinen TA, et al. Achilles tendinopathy. *J Bone Joint Surg Am* 2002;84-A(11):2062-76.

17. Cook J, Purdam C. Is compressive load a factor in the development of tendinopathy? *Br J Sports Med* 2012;46(3):163-68.

18. Kountouris A, Cook J. Rehabilitation of Achilles and patellar tendinopathies. *Best Pract Res Clin Rheumatol* 2007;21(2):295-316.

19. Kibler WB, Press J, Sciascia A. The role of core stability in athletic function. *Sports Med* 2006;36(3):189-98.

20. Bolgla LA, Malone TR, Umberger BR, et al. Comparison of hip and knee strength and neuromuscular activity in subjects with and without patellofemoral pain syndrome. *Int J Sports Phys Ther* 2011;6(4):285-96.

21. Ireland ML, Willson JD, Ballantyne BT, et al. Hip strength in females with and without patellofemoral pain. *J Orthop Sports Phys Ther* 2003;33(11):671-76.

22. Prins M, Van der Wurff P. Females with patellofemoral pain syndrome have weak hip muscles: a systematic review. *Austr J Phys* 2009;55(1):9-15.

23. Kulig K, Popovich JM, Jr., Noceti-Dewit LM, et al. Women with posterior tibial tendon dysfunction have diminished ankle and hip muscle performance. *J Orthop Sports Phys Ther* 2011;41(9):687-94.

24. Barwick A, Smith J, Chuter V. The relationship between foot motion and lumbopelvic-hip function: a review of the literature. *Foot* 2012;22(3):224-31.

25. McCrory JL, Martin DF, Lowery RB, et al. Etiologic factors associated with Achilles tendinitis in runners. *Med Sci Sports Exerc* 1999;31(10):1374-81.

26. Schepsis AA, Jones H, Haas AL. Achilles tendon disorders in athletes. *Am J Sports Med* 2002;30(2):287-305.

27. Lewis CL, Ferris DP. Walking with increased ankle pushoff decreases hip muscle moments. *J Biomech* 2008;41(10):2082-89.

28. Hutchison AM, Evans R, Bodger O, et al. What is the best clinical test for Achilles tendinopathy? *Foot Ankle Surg* 2013;19(2):112-17.

29. Konor MM, Morton S, Eckerson JM, et al. Reliability of three measures of ankle dorsiflexion range of motion. *Int J Sports Phys Ther* 2012;7(3):279-87.

30. Allen RH, Gross MT. Toe flexors strength and passive extension range of motion of the first metatarsophalangeal joint in individuals with plantar fasciitis. *J Orthop Sports Phys Ther* 2003;33(8):468-78.

31. Holm I, Bolstad B, Lütken T, et al. Reliability of goniometric measurements and visual estimates of hip ROM in patients with osteoarthrosis. *Physiother Res Int* 2000;5(4):241-48.

32. Roach S, San Juan JG, Suprak DN, et al. Concurrent validity of digital inclinometer and universal goniometer in assessing passive hip mobility in healthy subjects. *Int J Sports Phys Ther* 2013;8(5):680-88.

33. Thorborg K, Petersen J, Magnusson SP, et al. Clinical assessment of hip strength using a hand-held dynamometer is reliable. *Scand J Med Sci Sports* 2010;20(3):493-501.

34. Widler KS, Glatthorn JF, Bizzini M, et al. Assessment of hip abductor muscle strength. A validity and reliability study. *J Bone Joint Surg Am* 2009;91(11):2666-72.

35. Crossley K, Zhang WJ, Schache AG, et al. Performance on the single-leg squat task indicates hip abductor muscle function. *Am J Sports Med* 2011;39(4):866-73.

36. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

37. Faul F, Erdfelder E, Lang AG, et al. G*Power 3: A flexible statistical power analysis program fot the social, behavioral, and biomedical sciences. *Behavior Research Methods* 2007;39:175-91.

38. Heales LJ, Lim EC, Hodges PW, et al. Sensory and motor deficits exist on the non-injured side of patients with unilateral tendon pain and disability--implications for central nervous system involvement: a systematic review with meta-analysis. *Br J Sports Med* 2014;48(19):1400-06.

39. Stoll T, Huber E, Seifert B, et al. Maximal isometric muscle strength: normative values and gender-specific relation to age. *Clin Rheumatol* 2000;19(2):105-13.

40. Azevedo LB, Lambert MI, Vaughan CL, et al. Biomechanical variables associated with Achilles tendinopathy in runners. *Br J Sports Med* 2009;43(4):288-92.

41. Franettovich Smith MM, Honeywill C, Wyndow N, et al. Neuromotor control of gluteal muscles in runners with achilles tendinopathy. *Med Sci Sports Exerc* 2014;46(3):594-99.

42. Chuter VH, Janse de Jonge XAK. Proximal and distal contributions to lower extremity injury: a review of the literature. *Gait Posture* 2012;36(1):7-15.

43. Kulig K, Loudon J, Popovich J, et al. Dancers with achilles tendinopathy demonstrate altered lower extremity takeoff kinematics. *J Orthop Sports Phys Ther* 2011;41(8):606-13.

44. Williams DS, Zambardino JA, Banning VA. Transverse-plane mechanics at the knee and tibia in runners with and without a history of achilles tendonopathy. *J Orthop Sports Phys Ther* 2008;38(12):761-67.

45. Frontera WR, Hughes VA, Lutz KJ, et al. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol* 1991;71(2):644-50.

CHAPTER 7

Return to sport in athletes with midportion Achilles tendinopathy: a qualitative systematic review regarding definitions and criteria

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ABSTRACT

Background: Midportion Achilles tendinopathy (AT) can cause long-term absence from sports participation and shows high recurrence rates. It is important that the decision to return to sports (RTS) is made carefully, based on sharply delimited criteria. Lack of a well-defined definition and criteria hampers the decision to RTS among athletes with AT, and impedes comparison of RTS rates between different studies.

Objective: To systematically review the literature for definitions of, and criteria for, RTS in AT research.

Study Design: Qualitative systematic review.

Methods: We searched six databases (PubMed, EMBASE, Cochrane, CINAHL, PEDro, Scopus) for articles that reported on the effect of a physiotherapeutic intervention for midportion AT. Article selection was independently performed by two researchers. Qualitative content analysis was used to analyze the included studies and extract definitions of, and criteria for RTS.

Results: Thirty-five studies were included in the content analysis, showing large variety in both the definitions and criteria. Thirty-two studies reported a definition of RTS, but only 19 studies described criteria for RTS. The content analysis revealed that "reaching pre-injury activity/sports level, with the ability to perform training and matches without limitations", "absence of pain", and "recovery" were the main content categories used to define RTS. Regarding criteria for RTS, eight different content categories were defined: 1) "level of pain", 2) "level of functional recovery", 3) "recovery of muscle strength", 4) "recovery of range of motion", 5) "level of endurance of the involved limb", 6) "medical advice", 7) "psychosocial factors", and 8)" anatomical/physiological properties of the musculotendinous complex". Many criteria were not clearly operationalized and lacked specific information.

Conclusions: This systematic review shows that RTS may be defined according to the pre-injury level of sports (including both training and matches), but also with terms related to absence of pain and recovery. Multiple criteria for RTS were found, which were all related to level of pain, level of functional recovery, muscular strength, range of motion, endurance, medical advice, psychosocial factors, or anatomical/physiological properties of the Achilles tendon. For most of the criteria we identified, no clear operationalization was given, which limits their validity and practical usability. Further research on how RTS after midportion AT should be defined, and which criteria should be used, is warranted.

INTRODUCTION

Midportion Achilles tendinopathy (AT) can cause a prolonged absence from sports participation and may even be career-ending in up to 5% of the athletes with AT.[1] Recurrence rates as high as 27% have been reported, particularly in those with short recovery periods (0-10 days).[2] This might be related to the fact that, although symptoms have fully subsided, deficits in musculotendinous function may still persist in 25% of patients, putting the athlete at risk for re-injury.[3] Therefore, it is important that a decision on return to sport (RTS) is carefully made, based on multiple factors, and involving all relevant stakeholders.[4]

In a recent systematic review on eccentric training for midportion AT, performed by our research group,[5] we found that only one-third of the included studies used RTS as an outcome, with an RTS rate ranging between 10-86% after 12 weeks.[6 7] These studies used different definitions (e.g., "return to previous activity level" or "return to full activity"), which makes comparison of their RTS rates difficult. In many other AT studies, RTS is not the main outcome of the study, or it is not evaluated at all. This results in a lack of clear definition of RTS and an absence of well-defined criteria for RTS.

In 2016, a consensus statement on RTS after sports injuries was developed.[4] It stated that "the definition of each RTS process should, at a minimum, be according to the sport […] and the level of participation […] that the athlete aims to return to".[4] Silbernagel and Crossley[8] recently proposed a programme aimed at RTS for athletes with midportion AT. Whilst this programme provides a useful rationale and progression to RTS, unfortunately, the authors did not explicitly report a single clear definition of RTS, nor the exact criteria that should be met.

The lack of a clear definition and well-defined criteria can hamper the decision-making for RTS among athletes with AT. Moreover, it impedes comparison of RTS rates between different intervention studies. Therefore, the aim of this review was to systematically analyze the current literature for definitions of RTS in AT research, and investigate which criteria for RTS are being used.

METHODS

Study design

This systematic review was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and was prospectively registered in the PROSPERO database for systematic reviews (registration number CRD42017062518).

The purpose of the study was twofold: 1) to synthesize definitions of RTS, where RTS was seen a successful endpoint after midportion AT, and 2) to search for criteria used in scientific literature for decision-making to initiate RTS.

Search strategy

A systematic search of the literature from 1998 to July 2017 was conducted in PubMed, EMBASE, Cochrane, CINAHL, PEDro and Scopus. The search was limited from 1998 onwards based upon the paper from Maffulli et al.[9] According to this paper, the terminology changed from 'tendinitis', considered as a frank inflammation of the tendon, to 'tendinopathy', which is a combination of frequently longstanding pain, swelling and impaired performance.[9] This paradigm shift has led to changes in the management of tendinopathic injuries (i.e., targeted more at reducing symptoms and increasing load capacity rather than minimizing inflammation using non-steroid medication and/or injections), and this can have consequences for the factors associated with the RTS decision.

The search strategy contained various synonyms for "Achilles tendinopathy". For "return to sport", we partially adopted a search strategy used in a similar research on return to play after hamstring injuries,[10] and modified this to fit our study purpose. The final search strategy can be found in Electronic Supplementary Material Appendix S1.

Eligibility criteria

All retrieved articles were independently screened for eligibility by two authors (BHa, AB). All studies investigating the effect of any physiotherapeutic intervention in an adult (≥ 18 years) athletic population (i.e. individuals who participate in organized or non-organized sports) with midportion AT were eligible for inclusion, if they 1) described a definition of, and/or criteria for, RTS, and 2) were written in English, Dutch or German. There were no restrictions on type of study design. Articles that adopted definitions from other studies were excluded, but the studies from which the original definition was adopted were screened for eligibility, and included when they met our eligibility criteria. Potential articles were further excluded if they 1) were not available in full-text, despite serious efforts to contact the corresponding author, 2) described interventions for insertional AT and/or Achilles tendon rupture, 3) investigated surgical or other invasive interventions, or 4) were animal studies.

A consensus meeting between the two authors was held to discuss discrepancies in article screening and selection. If no consensus could be reached between the two authors, a third author (BHu) was asked to make a final decision. Cohen's kappa was calculated to indicate agreement between the two authors. A Cohen's kappa > 0.61 was considered as substantial agreement.

Data extraction

Two authors (BHa, AB) performed the data extraction from the included studies, using a standardized extraction form. The following relevant data were extracted: 1) first author, 2) year of publication, 3) study design, 4) study population, type and level of sport, 5) definition of the diagnosis of AT, 6) definition of RTS, 7) criteria described for initiation of RTS, and 8) recurrence rate and residual symptoms.

Data analysis

We searched for definitions of, as well as criteria for, RTS using a content analysis approach.[11-13] This is a qualitative method, aimed at classifying the written material into identified categories in three steps.[14] The first step of content analysis is open coding.[15] Two researchers (BHa, AB) independently read through the included studies several times, and started to identify provisional labels by making notes in the text indicating text fragments/aspects related to definitions of, or criteria for, RTS. A consensus meeting was conducted to compare the results of this step and discuss potential discrepancies.

The second step is axial coding; this aims to explore the relationships/associations among the provisional labels identified by open coding.[15] Both authors (BHa, AB) independently performed the axial coding process, and a consensus meeting was held afterwards to discuss potential discrepancies.

The third step of content analysis is selective coding.[15] During this step, the researchers aimed to develop overarching content categories that serve as umbrella terms for the labels identified during the axial coding phase. In the current review, the selective coding phase resulted in an overview of relevant terms that are used to define RTS after midportion AT, and the criteria that are used for the RTS decision.

RESULTS

Search results

The initial search yielded 3,862 hits (Figure 7.1). After removal of duplicates, 2,234 potential articles remained for inclusion. Screening of the titles and abstracts resulted in exclusion of another 2,039 articles, leaving 195 articles for full-text assessment. Of these, 10 (5%) could not be obtained in full-text, despite repeated attempts to contact the corresponding author by email or through ResearchGate, and despite attempts to purchase a copy. One hundred and thirty-four studies were excluded after full-text assessment. No consensus was reached on the eligibility of five articles. After consulting our third author (BHu), the studies by Cook et al.[16] and Herrington et al.[17] were included, while three other studies were excluded as they did not provide a definition of, or criteria for RTS.

Forty-eight articles met our inclusion criteria, but another 13 were excluded as they used a definition that was adopted from other studies. The studies containing the original definition were already included, so this resulted in a total of 35 articles that were included in the qualitative content analysis. These 35 studies included ten randomised controlled trials,

two non-randomised controlled trials, four pre-post studies, two retrospective cohort studies, one case series, two case studies, eight narrative reviews, four clinical commentaries, one masterclass report and one guideline report.
At this stage, Cohen's kappa was 0.69, indicating substantial agreement.[18]

Content analysis

Definition
Of the 35 included studies, 32 (91%) provided one or multiple definitions of RTS for athletes suffering from midportion AT. These definitions were extracted during the open coding phase of the content analysis (Table 7.1). During the axial coding phase, several categories were formed, which subsequently were grouped into three distinct content categories in the selective coding phase. These content categories were: "pre-injury activity/sports level, with the ability to perform training and matches without limitations", "absence of pain" and "recovery" (Figure 7.2).

• Reaching pre-injury activity/sports level, with the ability to perform training and matches without limitations

The majority of studies used terminology such as "return to/resume previous activity/sports level",[7 8 17 19-22] "return to pre-injury activity/sports level",[6 23-26] or "return to the original activity/sports level" [27-29] to define RTS. This finding was also reported in the included studies as "return to full (sports) activity",[8 21 30-32] "return to full training schedule without limitations",[28-33] and "return to competition".[16 23]

• Absence of pain

A few authors described "absence of pain" when defining RTS as follows: "pain-free return to activity",[34] "return to running without pain",[35] or "return the patient to the desired level of activity without residual pain".[36]

• Recovery

In terms of recovery, terminology used to define RTS included "risk of re-injury" (e.g., "safe return to sport while minimizing the risk of recurrent injury",[37] "returning to activity and avoiding repeated injury",[38] and "time to recovery", which was described as "swift return" [38] or "recovery time should be as short as possible".[36]

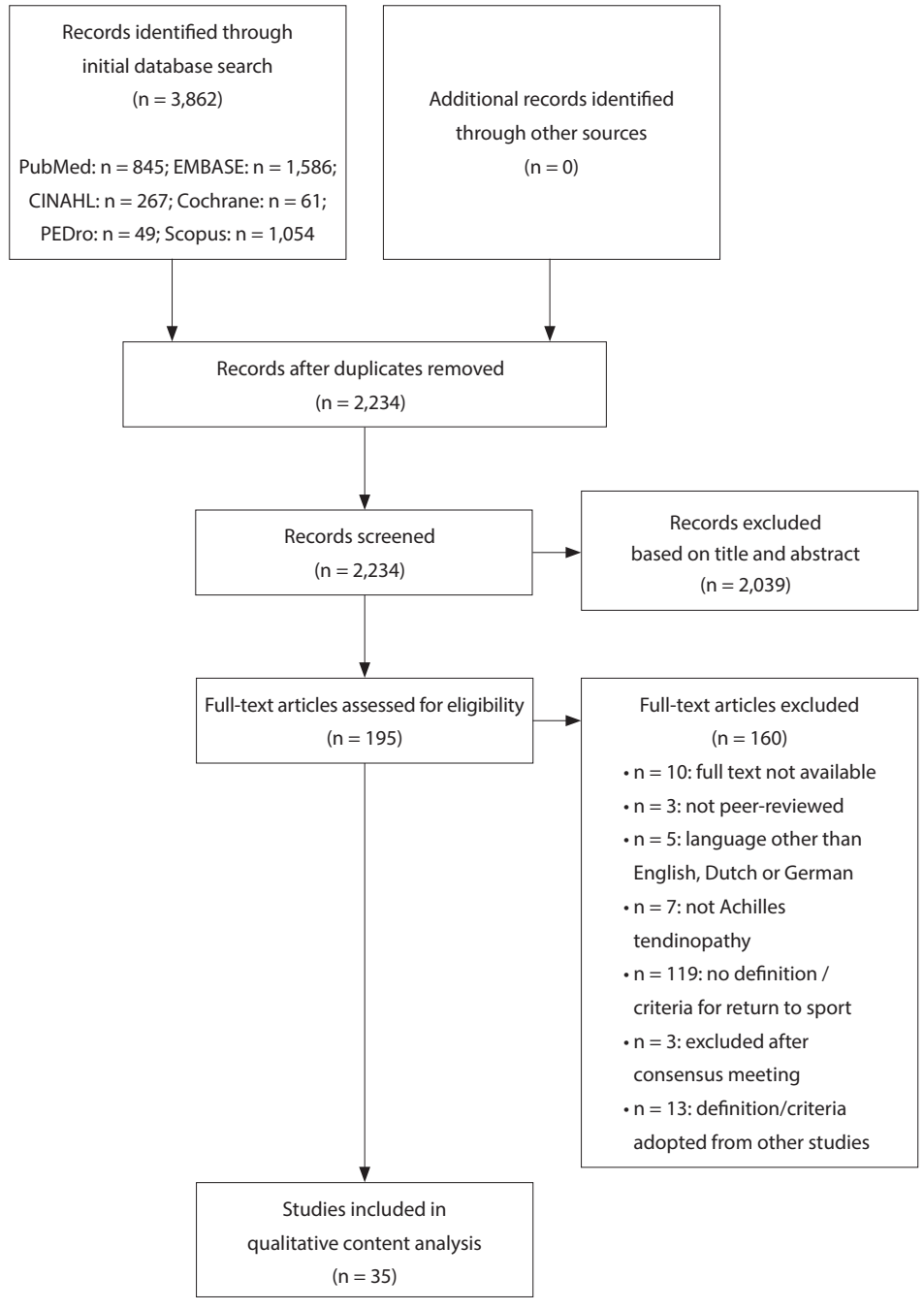

Figure 7.1 Flow chart of the search strategy

Criteria

Nineteen studies (54%) reported on one or more criteria for RTS after midportion AT (Table 7.1). Open coding resulted in different tentative labels, which were categorized during the axial coding phase. The final selective coding phase resulted in eight content categories (Figure 7.3).

• Level of pain

Large variation was seen in the included studies with regards to pain as a criterion for RTS. Some studies reported a complete absence of pain as a criterion for RTS, whereas other studies accepted a certain level of pain. One study reported that pain during sports activities should not exceed 30 mm on a 0-100 mm visual analog scale (VAS),[22] whilst other studies stated that daily activities should be pain-free,[35] or with minimal pain (1-2 on a 0-10 numerical pain rating scale)[8] before RTS can be considered.

• Level of functional recovery

Within the included studies, multiple aspects of functional recovery were described as criteria for RTS after AT. Nicola and El Shami reported that return to running should not be considered until one is able to walk comfortably at 4.0 mph for 10 miles per week,[35] whereas Werd stated that "RTS decisions should be based on "[…] the ability of the athlete to perform the necessary skills of the sport without restriction".[38]

• Recovery of muscular strength

In multiple studies, recovery of muscular strength was described as a criterion for RTS. Silbernagel and Crossley explicitly described that calf muscle weakness should be addressed before RTS,[8] but other studies did not explicate the muscle groups that should be addressed.

One study reported a limb symmetry index of 90% or more as a guideline for RTS,[39] whilst another study stated that recovery of strength to a level equal to the contralateral limb should be achieved.[38] No clear description was given of how muscle strength should be assessed.

• Recovery of range of motion

In four studies, range of motion was reported as a RTS criterion for AT, with one study specifying this as "mobility of the foot and ankle complex".[8] Werd used the contralateral limb as reference value ("equal to the contralateral limb"),[38] whereas other studies provided a more general description, such as "full range of motion".[37]

• Level of endurance of the involved limb

Endurance was addressed as a RTS criterion for AT in four of the included studies. Wetke et al. stated that jumping and running activities should be ceased until an athlete can perform three sets of 20 one-legged heel lifts on the stairs (without increased pain).[40]

Neither the required level of endurance nor the preferred measurement method were clearly specified in the other studies.[23 37 41]

• Medical advice

Several studies described that rehabilitation or a gradual stepwise training protocol should be completed prior to RTS,[8 23 38] yet the exact measurement method was not clearly described. In the study of Biedert et al.,[42] physical examination and specific tests were also mentioned as RTS criteria for AT. However, these were not further specified.

• Psychosocial factors

Psychosocial factors as criteria for RTS after AT were mentioned in one study.[42] The authors described that RTS depends on individual goals and mental aspects, but they did not further specify these factors.

• Anatomical/physiological properties of the musculotendinous complex

In three of the included studies, anatomical/physiological properties of the musculotendinous complex, specified as "structural healing",[42] "healing and recovery of the tendon tissue",[8] and "proprioceptive control" [41] were reported as criteria for RTS after AT. It was not clearly described how these properties were measured, for example, whether imaging was used to determine the recovery of tendon tissue.

Table 7.1 Definitions of, and criteria for RTS, as described in the included studies (similar to open coding of the content analysis)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Alfredson et al.[43]	CCT	15 athletes; 12 F, 3M; 44.3 ± 7.0 years; Recreational running 15 athletes; 4 F, 11 M; 39.6 ± 7.9 years; Recreational running and soccer	Achilles tendinosis: pain located in the Achilles tendon (2-6 cm above insertion on the calcaneus) for at least 3 months	Back at their pre-injury levels with full running activity Resumption of previous running activity	Running activity was allowed if it could be performed with only mild discomfort and no pain	RR not reported VAS mean 4.8/10 after returning to pre-injury activity level
Alfredson & Cook[20]	Narrative review	N/A	Achilles tendinopathy: Achilles mid-tendon pain, focal or generalized swelling	Back to previous tendon-loading activity level Back to previous activity level	Not reported	Both not reported
Ammendolia et al.[51]	RCT	19 athletes; sex not reported; 28.3 ± 4.9 years 16 athletes; sex not reported; 28.8 ± 4.4 years Elite volleyball	Overuse Achilles tendinitis	Resumption of training in the gym Return to play volleyball	Not reported	RR not reported VAS mean 3.8-4.9 when return to training in the gym VAS mean 0.6-2.4/10 when RTS
Barry[33]	Case study	1 M; 40 years Recreational running	Achilles tendinopathy	Returns to his training schedule without limitations	Not reported	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Beyer et al.[22]	RCT	25 athletes; 7 F, 18 M; 48 ± 2 years 22 athletes; 8 F, 14 M; 48 ± 2 years Recreational level, type not reported	Chronic unilateral midportion Achilles tendinopathy, based on: - Defined clinical findings (VISA-A score and VAS scale), physical examination, and pain duration of at least 3 months - US findings needed to be present: local A-P thickening of the midtendon level, with a hypoechoic area and a colour Doppler signal within the hypoechoic area	Resumed their previous activity levels	Sporting activities should be performed with a discomfort not exceeding 30 mm on the VAS	Both not reported
Biedert et al.[42]	Clinical commentary	N/A	Not reported	Return to physical fitness/former sport activities. Physical fitness can be divided into general and sports specific physical fitness. The authors further describe a stepwise progression from sports specific training to match specific training to match training.	The return to former sports activities depends on different factors such as structural healing, functional reintegration, physical examination, specific investigations and tests, as well as on individual goals and mental aspects.	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Chazan[30]	Narrative review	N/A	Achilles tendinitis, Achilles tendinosis	Return/resumption to full activity	Not reported	Both not reported
Chessin[41]	Narrative review	N/A	Achilles tendinitis: an inflammation of the tendon Achilles tendinosis: a chronic, non-inflammatory condition that is consistent with degenerated tissue and disorganised tendon structure.	Not reported	Capable of maintaining full dynamic load and controlling directional and speed changes with confidence. This requires progressive training for a balance of strength and flexibility, as well as building endurance and proprioceptive control	Both not reported
Chinn & Hertel[37]	Narrative review	N/A	Achilles tendonitis: an inflammatory condition that involves the Achilles tendon and/or its tendon sheath. Typically, the athlete will suffer from gradual pain and stiffness in the Achilles tendon region, 2 to 6 cm proximal to the calcaneal insertion	Full participation at full functioning Full competition Graduated return to physical activity Safe return to sport while minimizing the risk of recurrent injuries	Athletes should be allowed to compete when full range of motion and strength has returned. The athlete should have regained endurance in the involved limb and be capable of completing full practice without pain	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Cook et al.[16]	Masterclass report	N/A	Not reported	Return to training and competition	Inadequate amounts of load, speed and endurance may result in incomplete rehabilitation and insufficient musculotendinous function to return to sport	Both not reported
De Vos et al.[29]	RCT	32 athletic patients; 12 F, 20 M; 44.1 ± 7 years 31 athletic patients; 14 F, 17 M; 45.1 ± 8.9 years Recreational level, type not reported	Achilles tendinopathy: a tendon that was tender on palpation and painful during or after sport. The tendon thickening was located approximately 2-7 cm proximal to the distal insertion. Diagnosis was based on clinical examination	Return to their original level of sports	After 4 weeks, gradual return to sports activities was encouraged if the pain allowed it	Both not reported
Dijkstra & Van Enst[52]	Retrospective cohort study	9 patients; 4 F, 5 M; 43.2 (range 26-65) years Level not reported, athletics (n=6)	Achilles tendinosis; diagnosis based on history and clinical examination	Fully functioned at the original sports level	Not reported	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Fahlström et al.[19]	Pre-post study	78 patients; 25 F, 53 M; 46.1 ± 9.5 years Recreational level, running, walking and other sports	Chronic painful Achilles tendinosis at the midportion of the tendon (2-6 cm from the tendon insertion), with a duration of at least 3 months. Diagnosis based on clinical examination (painful nodular thickening of the Achilles tendon located at the level 2-6 cm from the tendon insertion) and US (local thickening of the tendon, irregular structure with hypo-echoic areas and irregular fibre orientation)	To return to previous (before injury) activity level Come back to previous (before injury) activity level To be able to participate in his/her desired sports/recreational activities Be fully active in their sport	During the 12-week training regimen, jogging/walking activity was allowed if it could be performed with only mild discomfort and no pain; patients were instructed to start jogging/walking at a slow pace, on flat ground, and for a short distance. Thereafter, their activity could be gradually increased if there was no severe pain in the tendon.	RR not reported VAS mean 10.2/100 after returning to previous activity level
Giombini et al.[26]	RCT	44 athletes; 11 F, 33 M; 26.0 ± 4.6 years Competitive level, type not reported	Achilles tendinopathy: pain and tenderness on palpation at the midportion of the tendon or at the distal insertion, associated with tendon swelling (diffuse or localized)	Full return to their pre-injury sport level A full return to sport; Return to specific sport activity	Not reported	RR not reported ~25% of athletes reported occasional discomfort after RTS

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Herrington et al.[17]	RCT	13 patients; sex not reported; 37.0 ± 9.3 years 12 patients; sex not reported; 36.6 ± 7.1 years Achilles loading sports, level and type not specifically reported	Non-insertional Achilles tendinopathy; local Achilles pain, stiffness or functional impairment on activity	Full return to the desired level of activity Full return to activity Returned to their previous activity levels	Not reported	Both not reported
Kountouris & Cook[23]	Narrative review	N/A	Achilles tendinopathy	Return to pre-injury levels of activity Return to competition	To achieve return to pre-injury activity levels, rehabilitation programme must incorporate some general principles of exercise programme design, such as strength, endurance, power, and a gradual return to sports-specific function	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Lakshmanan & Docherty[28]	Pre-post study	15 patients (16 tendons); 3 F, 12 M; 48.5 (range 35-77) years Active sports, level and type not specifically reported	Chronic non-insertional Achilles tendinopathy, for more than 6 months; diagnosis confirmed by US	Return back to their normal activities Return to full training activities with no limitation Returning back to the original level of physical activity in active sport persons Return back to their sports activities	Not reported	Both not reported
Langberg et al.[53]	CCT	6 patients; 6 M; 26 ± 1 year (the non-injured tendon served as a control) Elite soccer	Unilateral Achilles tendinosis: pain 30-60 mm above the Achilles tendon insertion on calcaneus	Return to the previous level of physical activity Back playing soccer	Subjects were allowed to continue soccer training if the pain had not increased	RR not reported VAS mean 13/100 after resuming soccer

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Mafi et al.[7]	RCT	22 patients; 10 F, 12 M; 48.1 ± 9.5 years 22 patients; 10 F, 12 M; 48.4 ± 8.3 years Recreational level, jogging and walking	Painful chronic Achilles tendinosis located at the 2-6 cm level in the tendon. Diagnosis based on clinical examination and US	Resumed their previous activity level (before injury)	During the 12-week training regimen, jogging/walking activity was allowed if it could be performed with only mild discomfort and no pain; Patients were instructed to start jogging/walking at a slow pace, on flat ground, and for a short distance. Thereafter, their activity could be gradually increased if there was no severe pain in the tendon	RR not reported VAS mean 9-12/100 after resuming previous activity level
McShane et al.[34]	Narrative review	N/A	Non-insertional Achilles tendinopathy	Pain-free return to activity; Back to their pre-injury level training regimen Returned to pre-injury training levels	Not reported	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Nicola & El Shami[35]	Clinical commentary	N/A	Midportion Achilles tendinopathy	Return to running without pain	Daily activities should be pain free before return to training For soft tissue injuries, there should be minimal residual tenderness In general, a period of 1 to 2 weeks of pain-free daily activities should be present before any consideration of return to running No running until patient able to walk comfortably at 4.0 mph for 10 miles per week	Both not reported
Paavola et al.[24]	Pre-post study	83 patients; 22 F, 61 M; 32 ± 11 years Competitive and recreational level, running and orienteering	A diagnosis of unilateral, nonchronic Achilles tendinopathy based on clinical examination (defined as exertional pain and palpable tenderness in the Achilles tendon of less than 6 months duration)	Returned to their pre-injury level of physical activity Fully recovered their physical activity level	Not reported	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Paavola et al.[36]	Review	N/A	Combination of Achilles tendon pain, swelling, and impaired performance	To return the patient to the desired level of physical activity without residual pain. In athletes, an additional demand is that the recovery time should be as short as possible Able to return to full levels of physical activity	Not reported	Both not reported
Petersen et al.[25]	RCT	37 patients; 14 F, 23 M; 42.5 ± 11.1 years 35 patients; 15 F, 20 M; 42.6 ± 10.7 years 28 patients; 11 F, 17 M; 43 ± 12 years Recreational level, running, walking and other sports	Gradually evolving painful condition in the Achilles tendon located at the midportion, for at least 3 months; diagnosis based on clinical examination and US	Return to pre-injury sports level Full recovery to previous activity level	Jogging, walking and bicycling were allowed if they could be performed with only mild discomfort or pain	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Rompe et al.[31]	RCT	25 patients; 16 F, 9 M; 48.1 ± 9.9 years 25 patients; 14 F, 11 M; 51.2 ± 10.3 years 25 patients; 16 F, 9 M; 46.4 ± 11.4 years Athletic patients, level and type not specifically reported	Pain over the main body of the Achilles tendon 2-6 cm proximal to its insertion, swelling and impaired function; clinical examination and US	Return to their normal levels of activity Return to full activity as possible	During the 12-week training regimen, jogging/walking activity was allowed if it could be performed with only mild discomfort and no pain; patients were instructed to start jogging/walking at a slow pace, on flat ground, and for a short distance. Thereafter, their activity could be gradually increased if there was no severe pain in the tendon	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Rompe et al.[21]	RCT	34 patients; 20 F, 14 M; 46.2 ± 10.2 years 34 patients; 18 F, 16 M; 53.1 ± 9.6 years Athletic patients, level and type not specifically reported	Pain over the main body of the Achilles tendon 2-6 cm proximal to its insertion, swelling and impaired function; clinical examination and US	Return to full activity Return to their previous sports/ recreational activity level	During the 12-week training regimen, jogging/walking activity was allowed if it could be performed with only mild discomfort and no pain; patients were instructed to start jogging/walking at a slow pace, on flat ground, and for a short distance. Thereafter, their activity could be gradually increased if there was no severe pain in the tendon.	Both not reported
Roos et al.[6]	RCT	44 patients; 23 F, 21 M; 46 (range 26-60) years Active in sport, level and type not specifically reported	Pain and swelling 2-6 cm proximal of the Achilles tendon insertion	Returned to their pre-injury activity level	Not reported	RR not reported 27-50% of patients reported moderate to extreme difficulties after returning to pre-injury activity level

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Ross et al.[54]	Case report	1 M; 23 years Semi-professional volleyball	Site of maximal tenderness 4 cm proximal to the Achilles insertion; clinical examination	Return to peak performance Return to volleyball Return to professional sport performance	Not reported	Both not reported
Silbernagel et al.[39]	Case series *(follow-up of a RCT)*	34 athletes; 16 F, 18 M; 51.0 ± 8.2 years Recreational level, type not specifically reported	Clinical diagnosis of a combination of Achilles tendon pain, swelling and impaired performance	Not reported	LSI below the level of 90% often used as a guideline for RTS	5/34 patients reported recurrence of symptoms after 5- year follow-up Symptoms: not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Silbernagel & Crossley[8]	Clinical commentary	N/A	Overuse injury, characterised by a combination of pain, swelling (diffuse or localized) and impaired performance; midportion Achilles tendinopathy is located 2-6 cm proximal to the insertion of the tendon on the calcaneus; based on history and physical examination	RTS with a low risk of re-injury or risk for other injuries RTS and previous activity level Back to sport participation; Full RTS Full sports participation Return to full sports activity	Resumption of activities such as running and jumping is generally recommended when the symptoms have subsided There are various factors that need to be considered when planning the return to sport after Achilles tendinopathy. The most obvious factor is the level of pain with physical activity. Other important factors that need to be included in the decision-making process are the healing and recovery of the tendon tissue, the recovery of strength, range of motion, and function; as well as the demands of the specific sport	Both not reported

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Silbernagel & Crossley[8] *(continued)*					RTS activity may be started prior to complete absence of symptoms Addressing calf muscle weakness and/or muscle imbalance, and altered joint mobility of the foot and ankle complex, with the aim of regaining full capacity, is important for athletes prior to full sports participation Return to full sports activity should involve gradual loading progression Knowledge of the rate and magnitude of Achilles tendon loads Before an athlete is allowed to return to any running or jumping activity, he or she should have minimal (1/10 to 2/10 on the NPRS) to no pain with all activities of daily living The RTS programme is initiated when the athlete meets the requirement of performing activities of daily living with pain no higher than 2/10	

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Sorosky et al.[44]	Clinical commentary	N/A	The combination of pain, swelling and impaired performance	Not reported	During the functional phase, jogging should be introduced gradually, increased only when there is no pain during or after exercise	Both not reported
Van Linschoten et al.[27]	Guideline report	N/A	Not reported	Return to the original level of sports	Not reported	Both not reported
Verrall et al.[32]	Retrospective cohort study	190 patients; 82 F, 108 M; 39 years Running and walking (n = 108), level not specifically reported	Tenderness on palpation and visible swelling of the mid-substance of the Achilles tendon; based on clinical assessment	Return to their preferred activity/ sport Return to full activity; Resumed unrestricted activity Resuming full activity but with some ongoing symptoms Return to their physical activity	Not reported	RR not reported 21% of patients had ongoing symptoms after return to full activity

Table 7.1 (continued)

Study	Study design	Population (n; sex; average age ± SD) Level and type of sport	Diagnosis	Definition of RTS	Criteria for RTS	RR Residual symptoms
Werd[38]	Narrative review	N/A	Not reported	Promptly returning to activity and avoiding repeated injury Safe and rapid return to activity Returning an injured athlete to sports as quickly and safely as possible	Return-to-play decisions should be based on an absence of pain, strength and range of motion equal to those of the contralateral limb, a gradual stepwise training protocol, and the ability of the athlete to perform the necessary skills of the sport without restriction	Both not reported
Wetke et al.[40]	Pre-post study	93 patients; 43 F, 52 (range 18-73) years; 50 M, 46 (range 21-73) years Active in sports, level and type not specifically reported	Local tenderness at palpation of tendon, tenosynovium or tendon insertion impairing the daily activities of the patient; clinical examination and US	Back to their former sports activity	All jumping and running exercises were paused until the patient could do 20 one-legged heel lifts on the stairs, in three series, without increased pain, and then walking/running activities were slowly resumed	Both not reported

RTS = return to sport; *RR* = recurrence rate; *SD* = standard deviation; *CCT* = clinically controlled trial; *F* = female; *M* = male; *N/A* = not applicable; *RCT* = randomised controlled trial; *VISA-A* = Victorian Institute of Sports Assessment – Achilles; *VAS* = visual analogue scale; *US* = ultrasound; *A-P* = anterior-posterior; *LSI* = limb symmetry index; *NPRS* = numerical pain rating scale

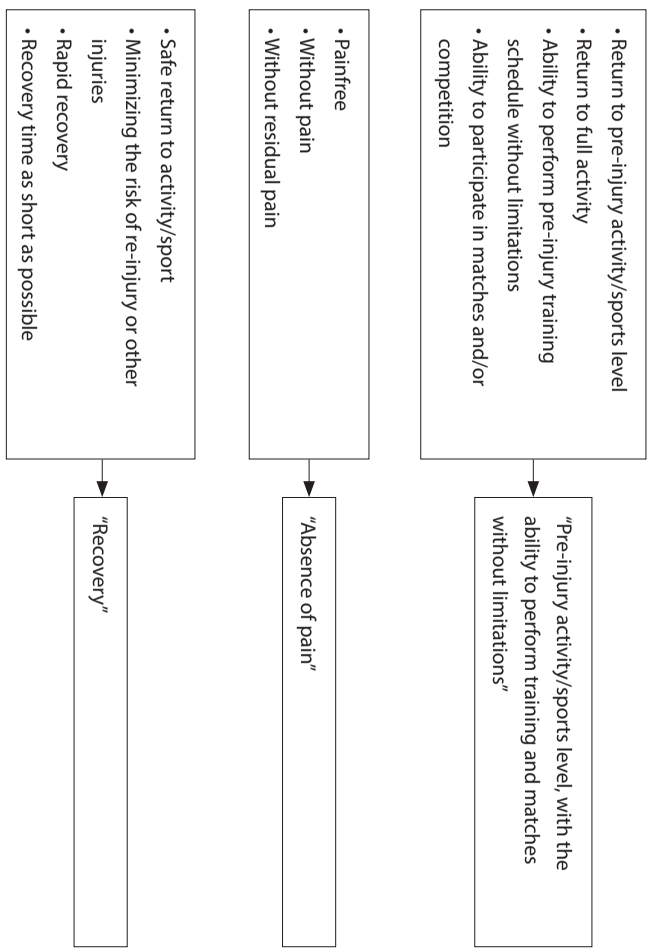

Figure 7.2 Axial coding and selective coding of the content analysis for the definition of return to sport after midportion Achilles tendinopathy

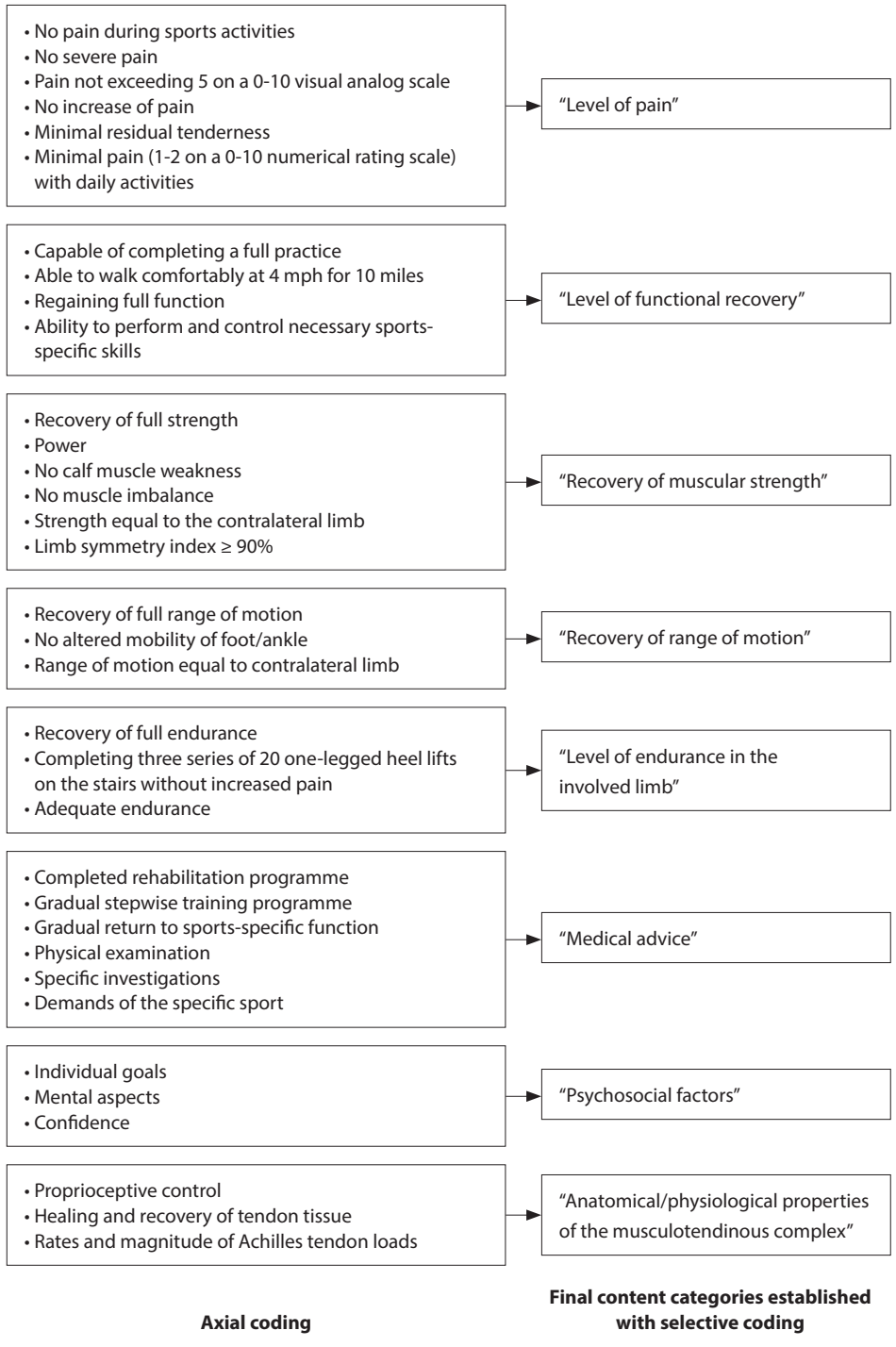

Figure 7.3 Axial coding and selective coding of the content analysis for criteria used for return to sport after midportion Achilles tendinopathy

DISCUSSION

RTS is an important goal for many athletes suffering from midportion AT, and the decision to RTS may be influenced by many factors. This qualitative systematic review aimed to describe how successful RTS after midportion AT is defined, and which criteria are used to support the RTS decision. Of the 35 studies included in this review, 91% provided a definition, and only 54% reported criteria for RTS after AT. We found large variation in definitions and criteria for RTS within the different studies. Using a content analysis approach, we aimed to discover content categories that serve as umbrella terms for the definition of, and criteria for RTS after midportion AT.

Definitions

Our content analysis approach identified three distinct content categories used to define successful RTS. Predominantly, we found that "pre-injury activity/sports level, with the ability to perform training and matches without limitations" seemed to be an important term. We also found that "absence of pain" and "recovery" (minimal risk of re-injury or other injuries, and time to recovery) were other important terms used to define RTS after midportion AT.

In a recent consensus statement on RTS after sports injuries in general,[4] it was stated that a RTS definition should, at a minimum, describe the type of sport and the sports level that is pursued. Many studies referred to the pre-injury level of sport of the involved athletes, but unfortunately, this level of sport was often not clearly described. Lack of clear description impedes comparison of pre-injury to post-injury RTS rates. Therefore, it will be beneficial to encourage studies to explicitly define the pre-injury sport and level of participation of their athletes. Ideally, this should be rated at baseline, or at least early during the intervention, to minimize recall bias of the participants.

Our results further show that, besides the type and level of sport, other relevant terms are also used to define RTS in the current AT literature. These terms were related to symptom level, time to recovery and risk of re-injury. This implies that merely returning to a certain level of sport is not enough; RTS should also be achieved in a timely manner and with minimal risk of re-injury.

Criteria

In total, 54% of the included studies described criteria for the RTS decision, but a large variation in these criteria was found. Using content analysis, we were able to define eight final content categories: 1) level of pain, 2) level of functional recovery, 3) recovery of muscle strength, 4) recovery of range of motion, 5) level of endurance of the involved limb, 6) medical advice, 7) psychosocial factors, and 8) anatomical/physiological properties of the musculotendinous complex.

Many studies described the level of pain as an important criterion for RTS. Seven studies stated that "no pain" should be present before RTS after midportion AT,[7 19 31 35 37 38 43 44] whereas others used less specific and subjective terms, such as minimal or mild pain/discomfort,[19 25 31 43] or no severe pain in the tendon.[7 19] Silbernagel and Crossley specified that the level of pain during daily activities should not exceed 2 on a 0-10 numerical pain scale before an athlete is allowed to return to running or jumping activities.[8] Beyer et al. also quantified the maximum level of pain that was allowed before RTS after AT,[22] but they specified it as pain during sports activities, and the level was slightly higher than the level used by Silbernagel and Crossley (i.e. 30 mm on a 0-100 mm VAS).

There is no doubt that pain is an important symptom of AT, and in particular morning pain/stiffness is a hallmark of AT. Morning pain/stiffness is considered as a useful clinical indicator of recovery,[16] and it has been included as part of the Victorian Institute of Sports Assessment – Achilles (VISA-A) questionnaire, which is considered a valid and reliable tool to evaluate AT symptoms.[45] Remarkably, none of the included studies explicitly described (absence of) morning pain/stiffness as a criterion for RTS. Furthermore, none of the studies used questionnaires such as the VISA-A as a criterion for RTS. It may be useful to investigate the possible role of the VISA-A in the decision to RTS among athletes with midportion AT, and to determine a cutoff score (e.g. ≥ 90 points)[46] as a required criterion for this decision.

Although many other criteria to support RTS after AT were described in the 35 included studies, it was remarkable that most of these criteria lacked essential information; the relevant body part was not described, no information on the preferred measurement method was given, or clear quantification or cutoff points were lacking. Regarding strength, for instance, studies reported information such as "balance of strength and flexibility" [41] or "when full strength has returned".[37] Only one study explicitly described the relevant muscle group (i.e. calf muscle),[8] and only the study by Silbernagel et al. reported a limb symmetry index of 90%,[39] which is often used as a reference for RTS in clinical practice. Furthermore, the vast majority of studies lacked information on which muscle groups should be tested (e.g. calf muscles, or all muscle groups of the lower extremity), what strength tests should be performed (e.g. isometric or isokinetic), which deficit between injured and uninjured limb is considered acceptable, and how this could be measured. This lack of information applied to most of the criteria found in this review. This obviously may result in a large variety of measures being used, thereby impeding the clinician's ability to make a well-considered and evidence-based decision on RTS. Additionally, it hampers comparison of RTS rates between different interventions for AT. Thus, we strongly encourage that studies comprehensively describe their criteria for RTS, and define clear cutoff values if possible. Furthermore, it would be of great interest when studies would also report the time to RTS, as this is of much importance for clinicians and other stakeholders involved in RTS decision-making.

Comparison with other findings

To our knowledge, this is the first systematic review investigating definitions and criteria for RTS in athletes with midportion AT, which limits the comparison with other findings. In the consensus statement on RTS after sports injuries, published by Ardern et al.,[4] RTS was described as a process using three elements: 1) return to participation, 2) return to sport, and 3) return to performance. We believe that this categorization of relevant elements has some advantages compared to our findings regarding the definition of RTS. We found "pre-injury level of activity/sports, with the ability to perform training and matches without limitations"to be an important term for defining successful RTS in our review, but this appears to refer to the end stage of a rehabilitation process. Using the proposed approach by Ardern et al.,[4] RTS is viewed more as a continuum, and this suggests that earlier in the process of rehabilitation, athletes may be active in their sport, albeit at a lower level and less intensity.

The consensus statement of Arden et al. further suggested that the rate of RTS after AT varies between 10-86% after 12 weeks of treatment.[4] The authors blame the variety of activity levels for the large variation in RTS rates. At present, we think that the lack of an unambiguous definition may also be responsible for this large variation; if studies interpret RTS differently, this poses difficulty in comparing the success rates for RTS.

Our review attempted to synthesize RTS after temporarily ceasing sports activities. This was in line with the findings of several studies, which reported that up to 72% of athletes with AT need to cease their sports activities due to ongoing symptoms.[29 32] However, research has demonstrated that completely ceasing sports activities may not be necessary. This point of view was based on a randomised controlled trial comparing two groups suffering from midportion AT.[47] The first group was allowed to engage in sports activities during the first six weeks of rehabilitation, using a pain-monitoring model. They were instructed that pain during sports activities should not exceed 5 on a 0-10 VAS, and that pain and stiffness in the Achilles tendon was not allowed to increase from week to week. The comparison group did not participate in Achilles tendon-loading sport for six weeks. As clinical improvement between both groups did not significantly differ, the authors concluded that continuing sports activities during rehabilitation using a pain-monitoring model is justified.[47] Although continuing sports activities using a pain-monitoring model may have advantages over temporary interruption (e.g. retaining tendon loading capacity and a positive effect on general health and psychological wellbeing), this decision should be made on an individual basis and consider factors such as level of symptoms and psychological factors.[48]

In a recent review of RTS after a rupture of the Achilles tendon,[49] the authors concluded that 80% (range 18.6 to 100%) of athletes returned to sport approximately six months after the injury. However, interestingly, both rate and time differed between the included studies that clearly described definitions and measures of return to play, and those stu-

dies that did not provide a description of how RTS was assessed.[49] These findings are in line with our results, namely, that there was a large variation in how RTS is defined, and many studies did not provide sufficient information on the type of measures that should be used to support the RTS decision. Therefore, we strongly advise both clinicians and researchers to achieve consensus, not only on a uniform definition for RTS after AT, but also to define what measures (physical tests, performance tests, questionnaires, psychological factors, imaging) should be included in order to make the RTS decision process more efficient and successful. As many criteria are interrelated, it would be worthwhile to consider grouping them together for clinical purpose. In future research, this may be addressed by performing a Delphi consensus strategy, similar to what was recently done for RTS after hamstring injuries.[50]

Strengths and limitations

A strength of this review is that it was conducted in accordance with the PRISMA guidelines, which enhances its methodological quality. Additionally, we made no restrictions on study design in our selection criteria. Whilst this may also be regarded as a limitation of the study, we feel that this decision maximized the chance of finding relevant literature on RTS after AT.

Our study also has some limitations that need to be addressed. First, a considerable proportion of studies (n = 10) could not be obtained in full text, despite serious efforts to contact the corresponding author of these studies (email, ResearchGate) to obtain a copy. These studies may have used different definitions and/or criteria for RTS, which could obviously have influenced our results. Secondly, although we did not place limitations on study design, we only included studies investigating the effects of physiotherapeutic interventions. Therefore, we do not know whether studies on medication, injection or operative treatments used different definitions and/or criteria.

CONCLUSION

This qualitative systematic review revealed a large variation within AT research in how RTS is defined and which criteria should be used to support the RTS decision. This limits the clinician's ability to make a well-considered RTS decision, and also hampers the comparison of RTS rates in different intervention studies. Using a content analysis approach, this systematic review showed that RTS may be defined according to the pre-injury level of sports (including both training and matches), but also with terms related to absence of pain and recovery.

Currently, RTS decisions for midportion AT seem to be based on multiple criteria, which are all related to level of pain, level of functional recovery, muscular strength, range of motion, endurance, medical advice, psychosocial factors, and anatomical/physiological properties of the Achilles tendon. It was remarkable that, for most of the criteria we identified, no clear operationalization was given, which limits their practical usability. Therefore, there is an urgent need for future research aiming to reach consensus on how RTS after midportion AT should be defined, and what criteria should be used to support the decision on RTS.

REFERENCES

1. Kvist M. Achilles tendon injuries in athletes. *Sports Med* 1994;18(3):173-201.

2. Gajhede-Knudsen M, Ekstrand J, Magnusson H, Maffulli N. Recurrence of Achilles tendon injuries in elite male football players is more common after early return to play: An 11-year follow-up of the UEFA Champions League injury study. *Br J Sports Med* 2013;47(12):763-8.

3. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med* 2007;41(4):276-80.

4. Ardern CL, Glasgow P, Schneiders A, Witvrouw E, Clarsen B, Cools A, et al. 2016 consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016 Jul;50(14):853-64.

5. Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: a systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.

6. Roos EM, Engstrom M, Lagerquist A, Soderberg B. Clinical improvement after 6 weeks of eccentric exercise in patients with mid-portion Achilles tendinopathy -- a randomized trial with 1-year follow-up. *Scand J Med Sci Sports* 2004 Oct;14(5):286-95.

7. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9(1):42-7.

8. Silbernagel KG, Crossley KM. A proposed return-to-sport program for patients with midportion Achilles tendinopathy: Rationale and implementation. *J Orthop Sports Phys Ther* 2015 Nov;45(11):876-86.

9. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: Time to change a confusing terminology. *Arthroscopy* 1998 Nov-Dec;14(8):840-3.

10. van der Horst N, van de Hoef S, Reurink G, Huisstede B, Backx F. Return to play after hamstring injuries: A qualitative systematic review of definitions and criteria. *Sports Med* 2016;46(6):899-912.

11. Cavanagh S. Content analysis: Concepts, methods and applications. *Nurse Res* 1997;4(3):5-16.

12. Krippendorff K. Content analysis: An introduction to its methodology. 2nd ed. Thousand Oaks: Sage Publications; 2004.

13. Elo S, Kyngas H. The qualitative content analysis process. *J Adv Nurs* 2008 Apr;62(1):107-15.

14. Moretti F, van Vliet L, Bensing J, Deledda G, Mazzi M, Rimondini M, et al. A standardized approach to qualitative content analysis of focus group discussions from different countries. *Patient Educ Couns* 2011 Mar;82(3):420-8.

15. Corbin J, Strauss A. Basics of qualitative research: Techniques and procedures for developing grounded theory. 4th ed. Thousand Oaks: Sage Publications; 2015.

16. Cook JL, Khan KM, Purdam C. Achilles tendinopathy. *Man Ther 2002* Aug;7(3):121-30.

17. Herrington L, McCulloch R. The role of eccentric training in the management of Achilles tendinopathy: A pilot study. *Phys Ther Spor.* 2007;8(4):191-6.

18. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977 Mar;33(1):159-74.

19. Fahlström M, Jonsson P, Lorentzon R, Alfredson H. Chronic Achilles tendon pain treated with eccentric calf-muscle training. *Knee Surg Sports Traumatol Arthrosc* 2003;11(5):327-33.

20. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: New treatment options. *Br J Sports Med* 2007;41(4):211-16.

21. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion Achilles tendinopathy: A randomized controlled trial. *Am J Sports Med* 2009 Mar;37(3):463-70.

22. Beyer R, Kongsgaard M, Hougs Kjaer B, Ohlenschlaeger T, Kjaer M, Magnusson SP. Heavy slow resistance versus eccentric training as treatment for Achilles tendinopathy: A randomized controlled trial. *Am J Sports Med* 2015;43(7):1704-11.

23. Kountouris A, Cook J. Rehabilitation of Achilles and patellar tendinopathies. *Best Pract Res Clin Rheumatol* 2007;21(2):295-316.

24. Paavola M, Kannus P, Paakkala T, Pasanen M, Jarvinen M. Long-term prognosis of patients with Achilles tendinopathy. an observational 8-year follow-up study. *Am J Sports Med* 2000;28(5):634-42.

25. Petersen W, Welp R, Rosenbaum D. Chronic Achilles tendinopathy: A prospective randomized study comparing the therapeutic effect of eccentric training, the AirHeel brace, and a combination of both. *Am J Sports Med* 2007 10;35(10):1659-67.

26. Giombini A, Di Cesare A, Casciello G, Sorrenti D, Dragoni S, Gabriele P. Hyperthermia at 434 MHz in the treatment of overuse sport tendinopathies: A randomised controlled clinical trial. *Int J Sports Med* 2002;23(3):207-11.

27. van Linschoten R, den Hoed PT, de Jongh AC. [Guideline 'Chronic Achilles tendinopathy, in particular tendinosis, in sportsmen/sportswomen']. *Ned Tijdschr Geneeskd* 2007;151(42):2319-24.

28. Lakshmanan P, O'Doherty DP. Chronic Achilles tendinopathy: Treatment with extracorporeal shock waves. *Foot Ankle Surg* 2004;10(3):125-30.

29. de Vos R, Weir A, Visser RJ, de Winter T, Tol JL. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: A randomised controlled trial. *Br J Sports Med* 2007 07;41(7):e5-.

30. Chazan IM. Achilles tendinitis part II: Clinical examination, differential diagnosis, and approaches to management. *J Man Manipul Ther* 1998;6(2):70-77.

31. Rompe JD, Nafe B, Furia JP, Maffulli N. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: A randomized controlled trial. *Am J Sports Med* 2007;35(3):374-83.

32. Verrall G, Schofield S, Brustad T. Chronic Achilles tendinopathy treated with eccentric stretching program. *Foot Ankle Int* 2011;32(9):843-49.

33. Barry M. Bringing Achilles tendinopathy to heel. *Nursing* 2010;40(10):30-33.

34. McShane JM, Ostick B, McCabe F. Noninsertional Achilles tendinopathy: Pathology and management. *Curr Sports Med Rep* 2007;6(5):288-92.

35. Nicola TL, El Shami A. Rehabilitation of running injuries. *Clin Sports Med* 2012;31(2):351-72.

36. Paavola M, Kannus P, Järvinen TA, Khan K, Józsa L, Järvinen M. Achilles tendinopathy. *J Bone Joint Surg* 2002;84-A(11):2062-76.

37. Chinn L, Hertel J. Rehabilitation of ankle and foot injuries in athletes. *Clin Sports Med* 2010;29(1):157-67.

38. Werd MB. Achilles tendon sports injuries: A review of classification and treatment. *J Am Podiatr Med Assoc* 2007;97(1):37-48.

39. Silbernagel KG, Brorsson A, Lundberg M. The majority of patients with Achilles tendinopathy recover fully when treated with exercise alone: a 5-year follow-up. *Am J Sports Med* 2011;39(3):607-13.

40. Wetke E, Johannsen F, Langberg H. Achilles tendinopathy: A prospective study on the effect of active rehabilitation and steroid injections in a clinical setting. *Scand J Med Sci Sports* 2015;25(4):e392-99.

41. Chessin M. Achilles tendinosis stopping the progression to disability. *J Dance Med Sci* 2012;16(3):109-15.

42. Biedert RM, Hintermann B, Hörterer H, Müller AE, Warnke K, Friederich N, et al. Return to sport after injuries and operative treatment. *Sport Orthop Sport Traumatol* 2006;22(4):249-54.

43. Alfredson H, Pietila T, Jonsson P, Lorentzon R. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998 May-Jun;26(3):360-66.

44. Sorosky B, Press J, Plastaras C, Rittenberg J. The practical management of Achilles tendinopathy. *Clin J Sport Med* 2004;14(1):40-44.

45. Robinson JM, Cook JL, Purdam C, Visentini PJ, Ross J, Maffulli N, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

46. Iversen JV, Bartels EM, Langberg H. The Victorian Institute of Sports Assessment - Achilles questionnaire (VISA-A) - A reliable tool for measuring Achilles tendinopathy. *Int J Sports Phys Ther* 2012;7(1):76-84.

47. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with Achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35(6):897-906.

48. Mallows A, Debenham J, Walker T, Littlewood C. Association of psychological variables and outcome in tendinopathy: A systematic review. *Br J Sports Med* 2017;51(9):743-48.

49. Zellers JA, Carmont MR, Gravare Silbernagel K. Return to play post-Achilles tendon rupture: a systematic review and meta-analysis of rate and measures of return to play. *Br J Sports Med* 2016;50(21):1325-32.

50. van der Horst N, Backx F, Goedhart EA, Huisstede BM, HIPS-Delphi Group. Return to play after hamstring injuries in football (soccer): A worldwide Delphi procedure regarding definition, medical criteria and decision-making. *Br J Sports Med* 2017;51(22):1583-91.

51. Ammendolia A, Cespites M, Iocco M. Topical use of aloe gel and low-level laser therapy in overuse tendinitis of elite volleyball players: A randomized controlled trial. *Sport Sci Health* 2016;12:209-13.

52. Dijkstra HJW, Van Enst GC. The therapeutic value of G-brace in the treatment of chronic Achilles tendinosis: A pilot study. *Geneeskunde & Sport* 2003;36(5):137-40.

53. Langberg H, Ellingsgaard H, Madsen T, Jansson J, Magnusson SP, Aagaard P, et al. Eccentric rehabilitation exercise increases peritendinous type I collagen synthesis in humans with Achilles tendinosis. *Scand J Med Sci Sports* 2007;17(1):61-66.

54. Ross G, Macfarlane C, Vaughan B. Combined osteopathy and exercise management of Achilles tendinopathy in an athlete: A case report. *J Sports Med Phys Fitness* 2018;58(1-2):106-112.

CHAPTER 8

General discussion

Despite a plethora of treatment options, successful treatment of midportion Achilles tendinopathy (AT) remains a challenge for both the clinician and the athlete. With our studies on the most effective loading programme, exploration of a possible role of the kinetic chain and defining successful return to sport (RTS) with well-defined criteria, we aimed to enlarge the evidence base for conservative treatment of midportion AT. In this way, this thesis aids clinicians in making an informed decision about adequate treatment strategies, helping them to obtain optimal treatment outcomes in their athletes with AT.
In this chapter, we discuss the main findings of this thesis as well as the limitations of our studies, and we provide recommendations for clinical practice and future research.

THE MOST EFFECTIVE LOADING PROGRAMME

Although the difference in effectiveness of loading compared to other treatments is somewhat ambiguous, it is considered an inexpensive therapy that can be easily implemented.[1] Furthermore, loading promotes self-efficacy during rehabilitation. Therefore, national and international guidelines recommend to commence treatment of AT with a loading intervention for at least 3 months[2 3] before considering other interventions, such as shockwave or injection therapy.[4-6] Nonetheless, the most effective loading programme remains elusive.[7 8] Identifying the most effective programme will help clinicians to offer a tailored treatment strategy to their patients instead of applying a one-size-fits-all approach for midportion AT.[9]

Based on the strong evidence for the effectiveness of eccentric loading of the plantar flexors found in previous studies,[5 10] we first conducted a systematic review **(Chapter 2)** focusing on this contraction mode. We found strong evidence for the original Alfredson programme, but our results also suggest that a gradual increase in exercises during the first week can be considered. The latter may be attractive to patients because it can prevent severe muscle soreness, which may affect exercise adherence. With the narrow scope of our review (i.e. eccentric loading), we did not include loading programmes using different contraction modes, although it has been suggested that these may yield equivalent effects.[8] Heterogeneity of outcome measures and study populations of the included studies in our review impeded us from performing a meta-analysis. Consequently, it was not possible to establish a precise treatment effect (effect size) for the different eccentric protocols, a fact that hampers comparison with published results of other loading interventions. Moreover, we were not able to determine the added value of loading against a natural course of AT, as only one included study compared eccentric loading (i.e. the Alfredson programme) to a wait-and-see approach.[11] Yet, based on the results of two recent meta-analyses, it can be assumed that exercise is superior to a wait-and-see approach after 3 months.[1 12]

Only one study included in our review compared the traditional Alfredson programme to a loading programme using concentric contractions.[13] The authors concluded that the Alfredson programme was superior, but in my opinion this conclusion is somewhat premature. There were some methodological shortcomings, such as the study design and a short follow-up term. Furthermore, Mafi et al.[13] included non-weight-bearing exercises in the concentric programme. It is likely that this approach generates inferior results when compared to full weight-bearing eccentric exercises.

In a randomised controlled trial (RCT) published after our review, Beyer et al.[14] demonstrated that heavy slow resistance training (HSRT), a combination of concentric and eccentric exercises performed on fitness equipment, showed equal beneficial clinical effects compared with the Alfredson programme in a population of physically active patients with midportion AT. Similar results were found in other tendinopathies, such as patellar and rotator cuff tendinopathy.[15-17] These findings challenge the superiority of eccentric loading over other contraction modes. This view is strengthened by previous research showing no discrepancy between concentric and eccentric loading in terms of tendon cellular response, even when the load for the eccentric exercises was set at 120% compared with the concentric exercises,[18] and similar expression of collagen after both concentric and eccentric loading.[19]

To further unravel the most effective loading programme, we conducted a single-blind RCT that compared eccentric loading according to the Alfredson protocol with a combination of concentric and eccentric loading according to the Silbernagel protocol **(Chapters 3, 4 and 5)**. Our RCT showed that both loading programmes yield beneficial effects, with significant improvement in symptoms and quality of life and increased lower extremity functional performance, but without a significant difference between the programmes.

As the training parameters proposed by Alfredson and colleagues are rather strict (e.g. exercising twice daily) and the programme offers limited variety, they may raise substantial issues regarding exercise adherence during the 12-week training period.[20] Indeed, studies that included adherence as an outcome only found good adherence (i.e. at least 75% of the prescribed exercises performed) in 27%-72% of the participants.[20-22] We expected that the Silbernagel programme, with a greater variety of exercises that should be performed only once daily, would demonstrate a higher adherence rate. Yet, interestingly, the adherence rate for Alfredson programme in our RCT was higher (74%) than found in other studies, and it was not inferior to the adherence rate for the Silbernagel programme (77%). The lack of a difference in the adherence rate supports that both programmes are well tolerated in a clinical setting. More specifically, as patients received only three instruction sessions by a physiotherapist, and they were largely self-responsible for completing the entire programme, the rather high adherence rates may even suggest that intensive supervision by a physiotherapist may not be required. In my clinical experience, patients are sometimes supervised on a weekly basis throughout the entire programme, but our

data suggest that is redundant. This is obviously beneficial from an economic perspective, given the increased spending on health care costs in the Netherlands.[23]

Our RCT used a multicentre approach, but we did not apply a stratification by centre. Two participating centres were sports medical centres, while the others were private clinics for physiotherapy. The patients seeking help from a sports physician may have a different profile – for example regarding activity level, origin and stage of the symptoms and treatment history – and this may have introduced systematic differences in the study population. Whilst these centre effects can potentially bias our study results, we did not consider them in our statistical analysis. Additionally, we refrained from an exploratory analysis of prognostic factors that predict the effectiveness of the loading interventions included in our RCT. Such an exploration could have facilitated clinicians in estimating a priori which programme will be the most effective based on specific characteristics of their athletes. Yet, our sample size was too small to allow for an appropriate multivariate analysis that reached sufficient statistical power. The limited sample size also impeded us from performing the cost-effectiveness analysis, which we intended to use.

Altogether, our research and previous studies indicate that the contraction mode may not be a key factor for the effectiveness of a loading programme. Other training parameters may be of more interest, but the ones that confer the greatest benefit are currently unknown.

Load intensity, volume (number of repetitions or sets), repetition duration (i.e. time under tension), frequency, the range of motion of the exercises, the rest period between each session and the duration of the entire programme are considered relevant characteristics to describe an exercise programme.[24] Of these, according to Bohm et al.,[25] high load intensity and prolonged time under tension are the most effective for an adaptive response of the tendon. This may be explained by the fact that higher loads and prolonged time during which these loads are imposed on the tendon (i.e. time under tension) produce a higher degree of tendon strain, resulting in tendon adaptation,[26] as well as increased tendon stiffness.[27 28] However, loads resulting in cyclic strains that are too large can result in tendon maladaptation.[29] The dosage that creates an optimal adaptive response may be influenced in tendinopathic tendons[29] and is equivocal.

A recent feasibility study by Hasani and colleagues[30] specifically investigated load intensity and time under tension in a sample of male patients with midportion AT. The participants were randomised into four groups that performed a plantar flexor strengthening programme with different load intensity and repetition duration: 6 repetition maximum (RM) for 6 s, 6 RM for 2 s, 18 RM for 6 s and 18 RM for 2 s. All groups showed a clinically relevant improvement on the Victorian Institute of Sports Assessment – Achilles (VISA-A) score, with the largest improvement reported for the group using low load and high time under tension (i.e. 18 RM for 6 s). Yet, given that this was a feasibility study, and the results were not statistically tested, a firm conclusion cannot be made.

Besides load intensity and time under tension, Bohm et al.[25] also concluded that the intervention duration can be a significant factor for tendon adaptation. Longer durations (i.e. > 12 weeks) were found to be more effective than shorter durations, probably due to greater improvement in tendon stiffness. Therefore, in my opinion, it is worthwhile to consider primarily load intensity, repetition duration and duration of the intervention as important loading principles when designing or prescribing loading interventions.

SELECTING AN APPROPRIATE PROGRAMME

According to the revisited continuum model, clinicians should distinguish the reactive and degenerative stages and a reactive-on-degenerative stage, which is a hybrid of reactive and degenerative pathology.[31] The reactive and reactive-on-degenerative stages are particularly characterised by a sudden onset of (severe) pain, cell proliferation and a fusiform swelling of the tendon.[32] Adequate load management is probably the first step to settle the reactive tendon and requires adaptation of provocative loads in terms of frequency, intensity, timing and type.[6 33] Subsequently, clinicians need to choose a loading programme that uses appropriate training parameters. This can be a delicate balance between minimising symptoms, avoiding overload of the tendon and a rapid return to full activity. There is no proven reason to advise against isolated eccentric loading in the reactive stage, but eccentric contractions may impose high peak loads on the tendon tissue, conceivably due to specific force fluctuations that occur.[34] These peak loads may not be desirable in a highly irritated tendon and may even cause symptoms to worsen.[35] Furthermore, in our clinical experience, it can be hard to convince patients that already have severe symptoms to perform painful exercises, a fact that may support not using heavy-load isolated eccentric loading in the reactive stage. Based on the findings of our RCT, a gradually progressed combination of concentric-eccentric contractions (i.e. the Silbernagel programme) may yield clinical effects comparable with eccentric loading. The Silbernagel programme may be more appropriate in the reactive stage because it uses a more gradual increase in the load (e.g. bilateral exercises on the floor level), thereby reducing the chance of overload and better allowing symptoms to settle. This also applies to the HSRT programme, which uses a gradual increase in the load and was found to be equally effective compared with eccentric loading.[14] Isometric loading is another option that can be considered in reactive AT. Isometric contractions do not involve any energy storage and release of the Achilles tendon and are therefore a safe option in this stage. They have been shown to result in immediate pain relief,[36-38] but as not all studies have shown good effects in AT,[39 40] this factor should be weighed for each individual. Moreover, the focus on quick pain relief may detract from the message that tendinopathy rehabilitation usually takes several months,[41] a factor that can possibly increase the chance of re-injury.

The degenerative stage is more common in older athletes and there is often less irritability of the tendon than in the reactive stage. Hence, isometric loading appears less relevant in the degenerative stage because immediate pain relief is less urgent. Optimising load tolerance of the tendon and restoring kinetic chain deficits can be considered the main goal of treatment and, in my view, this approach requires isotonic loading exercises that more closely resemble functional movements. Based on the current evidence, there is no reason to recommend one programme over another. The common features of the different loading programmes that predominantly seem to determine the clinical success are a gradual increase to a high load intensity, the usage of a pain-monitoring model, prolonged time under tension and a minimum training period of 12 weeks.[25 42] In my opinion, it is probably more important to implement these loading principles adequately rather than to prescribe the different loading programmes as a general recipe.

LOADING ALGORITHM

Whilst identifying one loading protocol that is appropriate for all patients is impossible, it seems useful to design a treatment algorithm that considers relevant criteria for selecting a loading intervention or loading principles. Although this could not be derived from our research, I would like to propose the algorithm given in Figure 8.1.

First, load intensity should be adjusted to the load tolerance of the tendon tissue, which is predominantly determined by the stage of tendinopathy. Second, patient characteristics, such as gender, age, body mass index (BMI) and athletic status, can direct the choice for a specific programme, as specific programmes tend to be less effective in certain subgroups. For example, with regard to eccentric loading, Knobloch et al.[43] demonstrated that it is more effective in male than in female patients. Furthermore, Sayana et al.[44 45] showed that athletic patients tend to have better results with eccentric loading than non-athletic patients. Conversely, eccentric loading was less effective in-season,[35] whilst slow-paced isotonic concentric-eccentric and isometric loading showed equally beneficial effects.[38] Hence, the choice for a specific loading programme may depend on whether an athlete is in-season.

Recent evidence suggests that compression between the Achilles tendon and the plantaris tendon during dorsiflexion occurs in some patients with AT, and this compression may have a role in the cause and the perseverance of their symptoms.[46 47] Therefore, in athletes in whom plantaris tendon involvement is suspected, adjusting the dorsiflexion angle during loading exercises should be considered, to prevent compressive forces between the Achilles and plantaris tendons. In this subgroup, I would advise to select a programme that initially involves less dorsiflexion during the exercises (like Phase 1 of the Silbernagel programme), or to temporarily adjust the dorsiflexion angle of the included exercises.

Lastly, other factors, such as patient preferences, motivation, time and previous experience with loading programmes need to be considered. For example, the Alfredson and Silbernagel programmes appear to be more appropriate for patients who prefer home-based rehabilitation, whilst patients who do not want to exercise daily and already exercise in a fitness centre on a regular basis may prefer the HSRT programme. Furthermore, patients that have tried one programme without satisfying results may still benefit from a different approach.

It should be emphasised that the proposed treatment algorithm is mainly based on clinical experience and lacks a broad scientific basis. The order of the criteria included in the algorithm is based on clinical reasoning, and different choices can be made. The development of an evidence-based treatment algorithm specifically designed for loading interventions for midportion AT clearly needs further investigation, which will be discussed in the future research section.

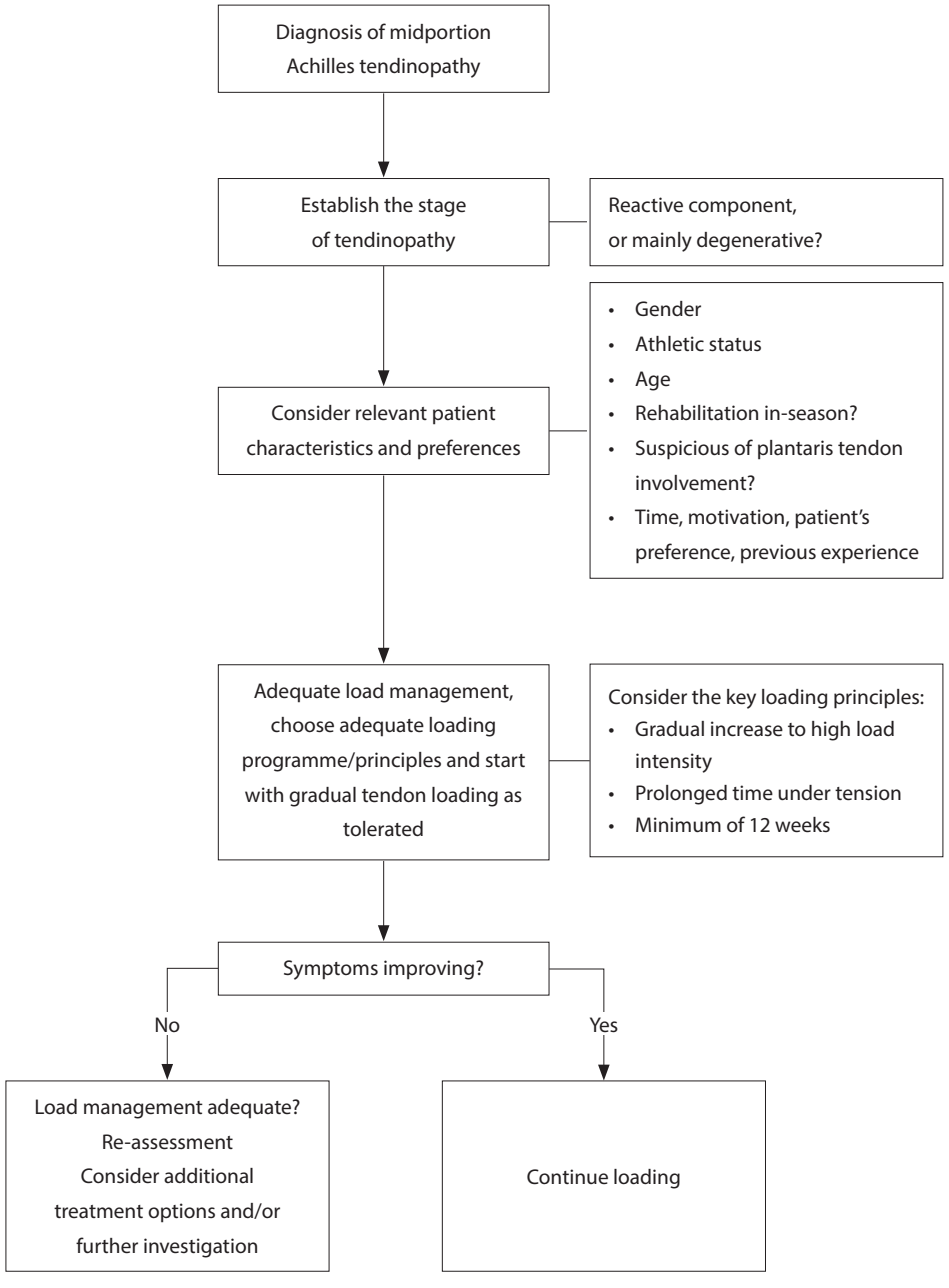

Figure 8.1 Algorithm for selecting an appropriate loading intervention for athletes with midportion AT

ROLE OF THE KINETIC CHAIN IN AT

Suboptimal functional performance of the lower extremity (e.g. hip and pelvic region) is thought to be a risk factor for various lower extremity injuries.[48-52] Furthermore, research has shown that optimising lower extremity function is an effective strategy for treating symptoms for some lower limb pathologies.[53 54] For midportion AT, the evidence for a link between injury (i.e. AT) and diminished functional performance of the lower extremity is less extensive.[55]

In our RCT **(Chapters 3, 4 and 5)**, we included several tests to assess functional performance of the lower limb. Our findings showed improved plantar flexor endurance in both programmes. Interestingly, we found that baseline differences between the injured and non-injured limb were completely resolved at 1-year follow-up. This is a remarkable finding, as previous research showed that functional deficits in the injured limb persisted after 1 year, despite full symptomatic recovery.[56] Nonetheless, it may be that comparison to the non-injured limb is inconvenient. In a group of athletes with midportion AT (N = 39), O'Neill et al.[57] demonstrated significant weakness of the plantar flexors, particularly in the soleus, in both the injured and non-injured limb compared with asymptomatic controls. Therefore, to draw a more robust conclusion on recovery of plantar flexor endurance in our RCT, comparison with matched healthy controls would have been more appropriate, but this endeavour would have required the inclusion of an additional study arm.

We also found that hip external rotator strength increased during the 1-year follow-up period. Improved hip external rotator strength can potentially improve disturbed lower limb kinematics such as increased internal rotation of the knee, which is seen in patients with AT,[58] but we did not specifically assess the latter in our RCT.

Contrary to improvement in hip strength and plantar flexor endurance, we found no improvement in jump height **(Chapter 5)**. This may be explained by the limited responsiveness of the countermovement jump, which we used to assess jump height. Inclusion of the drop countermovement jump or hopping might have been more opportune, as responsiveness of these tests was more promising.[59] Another explanation for the lack of improvement in jump height may be that, besides strength, jumping also requires other neuromuscular aspects, such as intermuscular coordination, peak power and rate of force development.[60] It is likely that these aspects are not sufficiently challenged with a loading programme solely targeted at the plantar flexors, irrespective of the contraction mode being used. Therefore, in my opinion, adequate rehabilitation of athletes with midportion AT should combine a specific plantar flexor loading programme with kinetic chain and gradually progressed sport-specific exercises, such as skipping, jumping and sprinting, as soon as symptoms allow. Incorporation of these exercises challenges the neuromuscular system of the entire kinetic chain, with greater chances of improving functional stretch-shortening-cycle tasks and better preparation for the RTS phase.[6] Sancho et al.[61]

investigated the effectiveness of such an approach in a recent feasibility study among 15 recreational runners with AT. The authors demonstrated that combining heel-raising exercises with a progressive hopping programme improved symptoms, plantar flexor and hip abductor strength as well as performance on a hopping test.

In a cross-sectional study, we specifically investigated hip muscle function in a sample of athletic patients with midportion AT **(Chapter 6)**. Our findings indicated considerable bilateral weakness of the hip extensors, abductors and external rotators, ranging from 28% to 34% compared with matched controls. Although the sample size and the cross-sectional nature of our study hinder us from drawing a conclusion on a causal relationship, our findings may justify that clinicians perform a specific assessment of hip muscle function in athletes with AT. We used a hand-held dynamometer, which is an easy and reliable method, but this solely provides insight into the level of isometric strength of an isolated muscle group instead of integral hip muscle function during (sport-specific) movement. Therefore, when symptoms allow, I would advocate the addition of a more functional evaluation of hip muscle performance, for example by using single leg balance and various hop tests.[62]

When profound strength deficits are found, several open and closed kinetic chain exercises can be offered at an early stage of the rehabilitation, particularly using positions that involve minimal energy storage and release of the Achilles tendon (e.g. single leg bridge, side-lying hip abduction, single-leg squat).[63 64] Once symptoms have settled and the load capacity of the tendon has improved, as previously discussed, kinetic chain exercises that involve higher levels of energy-storage-and-release, such as hopping, skipping, running and jumping) should be implemented.[65]

RTS AFTER MIDPORTION AT

The most important question an athlete will have during rehabilitation, irrespective of the treatment chosen, is probably when he/she will be able to resume previous sports activities. RTS is the ultimate goal of rehabilitation and can be considered the most demanding functional task for the Achilles tendon. Inadequate rehabilitation and forcing athletes to RTS prior to full recovery may put them at risk for re-injury. In athletes with AT, recurrence rates up to 27% have been published, with a higher re-injury rate (31%) reported after a short recovery period (0-10 days).[66]

An unambiguous definition of successful RTS, based on well-defined criteria, can help clinicians to determine when their athlete is ready to fully resume their sport. Furthermore, it promotes homogeneous evaluation of (end-stage) functional performance in intervention studies, enabling aggregated quantitative analysis of intervention effects.
In a qualitative systematic review **(Chapter 7)**, we found that a definition of successful RTS should be described around different aspects, that is, unrestricted participation at the

pre-injury sports level, absence of pain, time and minimal risk of re-injury. Yet, we were not able to synthesise an unambiguous definition from the literature, and this issue needs further investigation.

According to the consensus statement of Ardern et al.,[67] RTS can be considered a continuum with three important elements: return to participation, RTS and return to performance. The definition we synthesised in our review indicates the end stage of rehabilitation, equivalent to the return to performance stage of the RTS continuum of Ardern et al.[67] However, ideally this end stage is preceded by rehabilitation stages in which the tendon is gradually exposed to an increasing dosage of load by partial resumption of training and matches, and with careful monitoring of the response to the increased load.[6] The studies included in our review did not elaborate on these different stages. Hence, the clinical use of the definition found in our review may be hampered. It would be useful to reach a multidisciplinary consensus on an unambiguous definition that can be easily implemented in both research and clinical practice. This can probably be achieved with a Delphi consensus strategy, in which both health professionals and researchers are interrogated on this topic.[68] The advantage of a Delphi method is that it is anonymous[69] and that it combines the opinions of different experts whilst avoiding bias through status, dominant personality and institutional role.[70]

The most common criterion considered in RTS after AT is the level of pain; activities are often resumed once symptoms have fully subsided. However, given that full symptomatic recovery does not ensure full functional recovery,[6 56] the RTS decision should also involve other factors.
Our review showed a variety of criteria used to support the RTS decision. Besides the level of pain, these criteria were related to functional recovery, strength, endurance, range of motion, medical advice, psychosocial factors and tendon tissue properties.

According to the Strategic Assessment of Risk and Risk Tolerance (StARRT) framework developed by Shrier (see Figure 8.2),[71] most of the criteria found in our review can be considered medical factors that can help to appraise the athlete's (tissue) health status. Yet, assessment of medical factors forms only one part of the risk assessment.[71] Evaluation of sports risk modifiers (Step 2) and decision modifiers (Step 3) is also necessary to obtain a complete picture of the athlete. Sports risk modifiers relate to the characteristics of the sports activity (e.g. frequency, intensity, timing and type) and how they expose the injured Achilles tendon to stress. For example, a 5-km recreational runner (twice weekly) will experience different tendon loads compared with an elite sprinter (multiple sessions per day). In Step 3, the clinician considers the risk of re-injury against other factors that affect the overall health and wellbeing of the athlete. In this step, contextual factors, such as performance goals (e.g. participation in the coming Olympics) or financial agreements between the athlete and the sponsor(s) may ultimately change the balance of the RTS decision that was based on Steps 1 and 2. Our review did not provide information on criteria that relate to these last two steps.

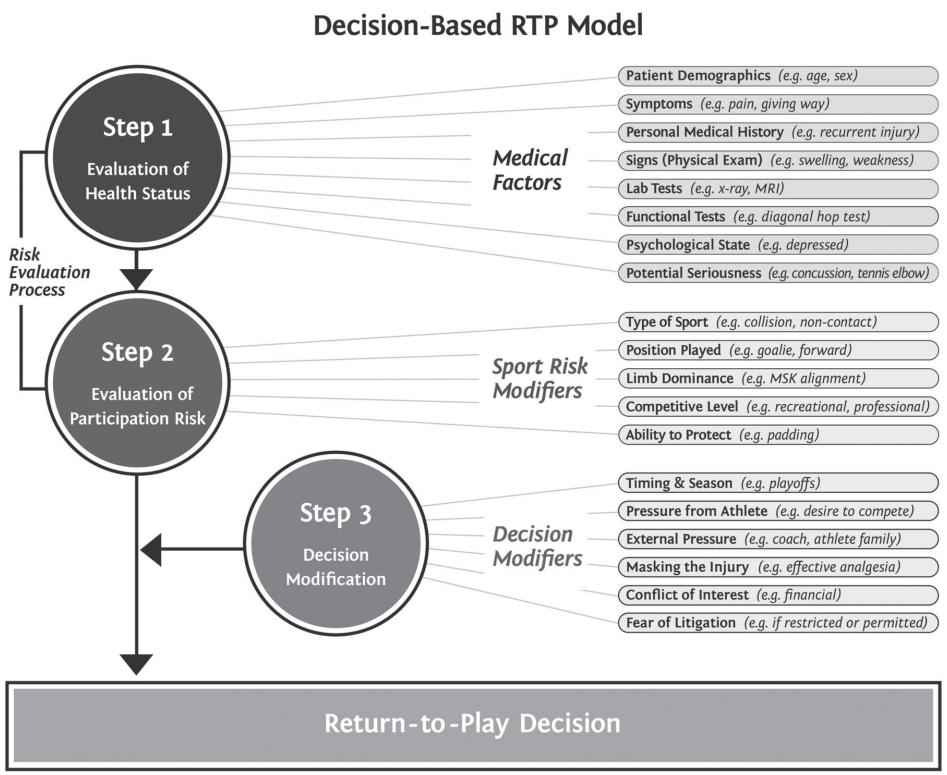

Figure 8.2 Strategic Assessment of Risk and Risk Tolerance (StARTT) framework for return to play decision by Shrier[71]

Since the publication of our review, a group of international health care professionals with broad experience in tendinopathy, together with a group of patients, has developed a consensus statement regarding core outcome domains for treatment of tendinopathy, by using a Delphi consensus strategy.[72] The recommended domains were 1) patient rating of the condition, 2) participation in activities, 3) pain on activity, 4) function, 5) psychological factors, 6) physical function capacity, 7) disability, 8) quality of life and 9) pain over a specified time. Interestingly, the consensus statement did not include domains such as range of motion, clinical examination and tendon structure, which were considered relevant factors in the studies we included in our review.

The consensus statement on core outcome domains was a first step towards a set of validated outcome measures. However, to date, such a set of outcome measures with well-defined cut-off values is lacking, which is in line with the findings of our review. Until consensus is reached, clinicians should use several outcome measures to support their decision-making, although I acknowledge that not all outcome domains may be covered and the demanded scores for the RTS decision are mostly lacking.

The VISA-A score is probably the most convenient questionnaire to assess the patient's rating of their condition, based on its adequate psychometric properties.[73 74] According to previous research, a score of ≥ 90 points on the VISA-A is considered full recovery[75] and may therefore be sufficient for RTS.

Regarding physical function capacity, several aspects of lower limb functional performance can be evaluated by the test battery developed by Silbernagel et al.[59]; it was found to be reliable and includes measures of plantar flexor muscle function (i.e. strength and endurance) and assessment of energy-storage-and-release activities such as jumping and hopping. A limb symmetry index (i.e. the ratio between the injured and the non-injured limb, defined as a percentage) > 90% is considered normal for this test battery,[59] but as previously mentioned, it is questionable whether the uninjured limb is appropriate for comparison. Plantar flexor strength and endurance can also be assessed using isokinetic dynamometry, but this requires expensive equipment.[74]

Psychological factors have gained increased attention in AT in recent years.[76 77] Based on the limited evidence available, the Tampa Scale of Kinesiophobia may be used to assess fear of pain with movement, which is not uncommon in patients with AT.[30] Additionally, in our RCT **(Chapter 4)**, we used the Euroqol instrument (EQ-5D) to evaluate quality of life. Although we did not establish the psychometric properties of the EQ-5D in athletes with AT, we found that several athletes experienced problems with quality of life. Other questionnaires may be available, but the EQ-5D offers a compact assessment of this domain and is easy to implement in a clinical setting. To the best of my knowledge, no data are available on which scores should be obtained before RTS after midportion AT.

CLINICAL IMPLICATIONS

The aim of this thesis was to enlarge the evidence base for conservative treatment of midportion AT in athletes. Based on our research, the following advice for clinical practice can be given.

- When clinicians prefer to prescribe an isolated eccentric loading programme to their athletes, the original Alfredson programme is the most effective protocol. Using a gradual onset of exercises during the first week does not alter the effectiveness, but it may prevent severe muscle soreness in the plantar flexors.
- Both the Alfredson and the Silbernagel loading programmes yield significant improvement in symptoms during a 1-year follow-up period, and these effects tend to be similar between the programmes. Based on these findings, the state-of-the-art treatment approach using eccentric loading according to the Alfredson programme within recreational athletes with midportion AT should be questioned, and the relevance of the contraction mode in the rehabilitation of AT may be challenged.

- Plantar flexor endurance can be restored to the level of the non-injured limb at 1-year follow-up after following a loading programme according to the Alfredson or the Silbernagel protocol.

- When prescribed as home-based exercise programmes with minimal supervision from a physiotherapist, the Alfredson and Silbernagel programmes show similar good adherence rates. As most participants showed clinically relevant improvement with minimal supervision, standard intensive supervision of recreational athletes with midportion AT can be questioned.

- Clinicians should be aware that impaired functional performance of the lower extremity, such as pronounced strength deficits of the hip muscle groups, may be present in recreational athletic patients with AT. Both the Alfredson and Silbernagel loading programmes improve aspects of functional performance of the lower limb (i.e. plantar flexor endurance and hip external rotator strength), but translation into functional tasks appears limited.

- Successful RTS in AT is achieved when an athlete is able to participate in training and matches at the pre-injury level without restrictions and with minimal risk of re-injury.

- Clinicians who aim to assess whether athletes are ready to RTS should consider assessment on the domains of symptoms (pain), functional performance, psychosocial health and medical advice. Unfortunately, because the current evidence lacks information on outcome measures and cut-off values, a set of uniform and well-defined criteria cannot be recommended.

FUTURE PERSPECTIVES

Several aspects of the conservative treatment of midportion AT have been discussed in this thesis. However, various questions are still unanswered and new questions have emerged. I feel that the following topics should be further uncovered in future research.

Loading interventions

There remains uncertainty on which loading programme or loading principles confer the best effects. Adequately powered prospective clinical trials comparing training parameters, such as load magnitude, repetition duration and duration of the programme, are needed to obtain insight into optimal dose-response relationships. These studies should specify their population (reactive/degenerative tendinopathy) and include outcome measures that aid in understanding the underlying mechanism of action (e.g. tendon adaptation, or neuromuscular or psychological improvement).

The proposed treatment algorithm in this thesis was a first step towards a clinical tool that can help clinicians in selecting an appropriate programme based on specific characteristics of their athletes instead of providing one-size-fits-all care. A Delphi study can hopefully yield consensus among tendon experts on relevant predictors that should be implemented in an algorithm, which would then require validation.

Functional performance

Well-designed and adequately powered prospective cohort studies are needed to investigate the link between decreased functional performance of the lower leg and AT. When measures of functional performance, such as decreased plantar flexor strength, impaired hip muscle function or impaired jumping/hopping performance, are found to be risk factors for midportion AT, this can be used to design adequate preventive training programmes. Based on the current state of knowledge, we also advise that a clinical trial comparing a plantar flexor loading programme with a similar programme supplemented with exercises of proximal muscle groups and gradually progressed SSC exercises is performed in the future.

RTS

The lack of an unambiguous definition of RTS in midportion AT hampers the comparability of different interventions. Thus, there is a strong need for an unambiguous definition as well as for set of validated outcome measures that help to determine when an athlete is ready to fully resume sports activities. A Delphi study will hopefully yield consensus on a definition as well as a set of well-defined criteria among a group of tendon experts (researchers and health care professionals). Subsequently, an adequately powered validation study needs to be conducted to verify whether these outcome measures can indeed predict a safe RTS after midportion AT.

Although this thesis can contribute substantially to the knowledge on loading programmes, hip muscle dysfunction and return to sport in athletes with midportion AT, clinicians should acknowledge that successful treatment can still be a challenge. Future steps are needed to expand knowledge on predictors that can be used for choosing an appropriate treatment strategy and selecting appropriate outcome measures. This will help clinicians to obtain optimal treatment results for their athletes with midportion AT.

REFERENCES

1. van der Vlist AC, Winters M, Weir A, et al. Which treatment is most effective for patients with Achilles tendinopathy? A living systematic review with network meta-analysis of 29 randomised controlled trials. *Br J Sports Med* 2021;55(5):249-56.
2. Martin RL, Chimenti R, Cuddeford T, et al. Achilles pain, stiffness, and muscle power deficits: Midportion Achilles tendinopathy revision 2018. *J Orthop Sports Phys Ther* 2018;48(5):A1-A38.
3. De Vos RJ, Van der Vlist AC, Zwerver J, et al. Dutch multidisciplinary guideline on Achilles tendinopathy. *Br J Sports Med* 2021 doi: 10.1136/bjsports-2020-103867 [published Online First: 29 June 2021]
4. Alfredson H, Cook J. A treatment algorithm for managing Achilles tendinopathy: new treatment options. *Br J Sports Med* 2007;41(4):211-16.
5. Sussmilch Leitch SP, Collins NJ, Bialocerkowski AE, et al. Physical therapies for Achilles tendinopathy: systematic review and meta-analysis. *J Foot Ankle Res* 2012;5(1):15.
6. Silbernagel KG, Crossley KM. A proposed return-to-sport program for patients with midportion Achilles tendinopathy: Rationale and implementation. *J Orthop Sports Phys Ther* 2015;45(11):876-86.
7. Meyer A, Tumilty S, Baxter GD. Eccentric exercise protocols for chronic non-insertional Achilles tendinopathy: how much is enough? *Scand J Med Sci Sports* 2009;19(5):609-15.
8. Malliaras P, Barton C, Reeves N, et al. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43(4):267-86.
9. Silbernagel KG. Does one size fit all when it comes to exercise treatment for Achilles tendinopathy? *J Orthop Sports Phys Ther* 2014;44(2):42-4.
10. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. *Sports Med* 2012;42(11):941-67.
11. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: A randomized controlled trial. *Am J Sports Med* 2007;35(3):374-83.
12. Murphy MC, Travers MJ, Chivers P, et al. Efficacy of heavy eccentric calf training for treating mid-portion Achilles tendinopathy: a systematic review and meta-analysis. *Br J Sports Med* 2019;53(17):1070-7.
13. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9(1):42-47.
14. Beyer R, Kongsgaard M, Hougs Kjaer B, et al. Heavy slow resistance versus eccentric training as treatment for Achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2015;43(7):1704-11.
15. Kongsgaard M, Qvortrup K, Larsen J, et al. Fibril morphology and tendon mechanical properties in patellar tendinopathy: effects of heavy slow resistance training. *Am J Sports Med* 2010;38(4):749-56.
16. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports* 2009;19(6):790-802.

17. Dejaco B, Habets B, van Loon C, et al. Eccentric versus conventional exercise therapy in patients with rotator cuff tendinopathy: a randomized, single blinded, clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2017;25(7):2051-59.
18. Farup J, Rahbek SK, Vendelbo MH, et al. Whey protein hydrolysate augments tendon and muscle hypertrophy independent of resistance exercise contraction mode. *Scand J Med Sci Sports* 2014;24(5):788-98.
19. Heinemeier KM, Olesen JL, Haddad F, et al. Expression of collagen and related growth factors in rat tendon and skeletal muscle in response to specific contraction types. *J Physiol* 2007;582(Pt 3):1303-16.
20. Roos EM, Engstrom M, Lagerquist A, et al. Clinical improvement after 6 weeks of eccentric exercise in patients with mid-portion Achilles tendinopathy -- a randomized trial with 1-year follow-up. *Scand J Med Sci Sports* 2004;14(5):286-95.
21. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med* 2011;45(5):421-28.
22. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41(7):e1-e6.
23. van Weel C, Knottnerus JA, van Schayck OCP. Managing costs and access to healthcare in the Netherlands: impact on primary care. *BMJ* 2020;369:m1181.
24. Couppe C, Svensson RB, Silbernagel KG, et al. Eccentric or concentric exercises for the treatment of tendinopathies? *J Orthop Sports Phys Ther* 2015;45(11):853-63.
25. Bohm S, Mersmann F, Arampatzis A. Human tendon adaptation in response to mechanical loading: a systematic review and meta-analysis of exercise intervention studies on healthy adults. *Sports Med Open* 2015;1(1):7.
26. Arampatzis A, De Monte G, Karamanidis K, et al. Influence of the muscle-tendon unit's mechanical and morphological properties on running economy. *J Exp Biol* 2006;209(Pt 17):3345-57.
27. Malliaras P, Kamal B, Nowell A, et al. Patellar tendon adaptation in relation to load-intensity and contraction type. *J Biomech* 2013;46(11):1893-9.
28. Kongsgaard M, Reitelseder S, Pedersen TG, et al. Region specific patellar tendon hypertrophy in humans following resistance training. *Acta Physiol (Oxf)* 2007;191(2):111-21.
29. Docking SI, Cook J. How do tendons adapt? Going beyond tissue responses to understand positive adaptation and pathology development: A narrative review. *J Musculoskelet Neuronal Interact* 2019;19(3):300-10.
30. Hasani F, Haines T, Munteanu SE, et al. LOAD-intensity and time-under-tension of exercises for men who have Achilles tendinopathy (the LOADIT trial): a randomised feasibility trial. *BMC Sports Sci Med Rehabil* 2021;13(1):57.
31. Cook JL, Rio E, Purdam CR, et al. Revisiting the continuum model of tendon pathology: what is its merit in clinical practice and research? *Br J Sports Med* 2016;50(19):1187-91.

32. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. *Br J Sports Med* 2009;43(6):409-16.

33. Mascaró A, Cos MA, Morral A, et al. Load management in tendinopathy: clinical progression for Achilles and patellar tendinopathy. *Apunts Med Esport* 2018;53(197):19-27.

34. Rees JD, Lichtwark GA, Wolman RL, et al. The mechanism for efficacy of eccentric loading in Achilles tendon injury an in vivo study in humans. *Rheumatology* 2008;47(10):1493-97.

35. Visnes H, Hoksrud A, Cook J, et al. No effect of eccentric training on jumper's knee in volleyball players during the competitive season: a randomized clinical trial. *Clin J Sport Med* 2005;15(4):227-34.

36. Bradford B, Rio E, Murphy M, et al. Immediate effects of two isometric calf muscle exercises on mid-portion Achilles tendon pain. *Int J Sports Med* 2021 doi: 10.1055/a-1398-5501 [Epub ahead of print].

37. Rio E, Kidgell D, Purdam C, et al. Isometric exercise induces analgesia and reduces inhibition in patellar tendinopathy. *Br J Sports Med* 2015;49(19):1277-83.

38. van Ark M, Cook JL, Docking SI, et al. Do isometric and isotonic exercise programs reduce pain in athletes with patellar tendinopathy in-season? A randomised clinical trial. *J Sci Med Sport* 2016;19(9):702-6.

39. van der Vlist AC, van Veldhoven PLJ, van Oosterom RF, et al. Isometric exercises do not provide immediate pain relief in Achilles tendinopathy: A quasi-randomized clinical trial. *Scand J Med Sci Sports* 2020;30(9):1712-21.

40. O'Neill S, Radia J, Bird K, et al. Acute sensory and motor response to 45-s heavy isometric holds for the plantar flexors in patients with Achilles tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2019;27(9):2765-73.

41. Gravare Silbernagel K, Vicenzino BT, Rathleff MS, et al. Isometric exercise for acute pain relief: is it relevant in tendinopathy management? *Br J Sports Med* 2019;53(21):1330-31.

42. Malliaras P, Rodriguez Palomino J, Barton CJ. Infographic. Achilles and patellar tendinopathy rehabilitation: strive to implement loading principles not recipes. *Br J Sports Med* 2018;52(19):1232-33.

43. Knobloch K, Schreibmueller L, Kraemer R, et al. Gender and eccentric training in Achilles mid-portion tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2010;18(5):648-55.

44. Maffulli N, Walley G, Sayana MK, et al. Eccentric calf muscle training in athletic patients with Achilles tendinopathy. *Disabil Rehabil* 2008;30(20-22):1677-84.

45. Sayana M, Maffulli N. Eccentric calf muscle training in non-athletic patients with Achilles tendinopathy. *J Sci Med Sport* 2007;10(1):52-8.

46. Masci L, Spang C, van Schie HT, et al. How to diagnose plantaris tendon involvement in midportion Achilles tendinopathy - clinical and imaging findings. *BMC Musculoskelet Disord* 2016;17:97.

47. Spang C, Alfredson H, Docking SI, et al. The plantaris tendon: a narrative review focusing on anatomical features and clinical importance. *Bone Joint J* 2016;98-B(10):1312-9.

48. Leetun DT, Ireland ML, Willson JD, et al. Core stability measures as risk factors for lower extremity injury in athletes. *Med Sci Sports Exerc* 2004;36(6):926-34.

49. De Blaiser C, De Ridder R, Willems T, et al. Impaired core stability as a risk factor for the development of lower extremity overuse injuries: A prospective cohort study. *Am J Sports Med* 2019;47(7):1713-21.

50. Mucha MD, Caldwell W, Schlueter EL, et al. Hip abductor strength and lower extremity running related injury in distance runners: A systematic review. *J Sci Med Sport* 2017;20(4):349-55.

51. Niemuth PE, Johnson RJ, Myers MJ, et al. Hip muscle weakness and overuse injuries in recreational runners. C*lin J Sport Med* 2005;15(1):14-21.

52. Khalaj N, Vicenzino B, Heales LJ, et al. Is chronic ankle instability associated with impaired muscle strength? Ankle, knee and hip muscle strength in individuals with chronic ankle instability: a systematic review with meta-analysis. *Br J Sports Med* 2020;54(14):839-47.

53. Santos TR, Oliveira BA, Ocarino JM, et al. Effectiveness of hip muscle strengthening in patellofemoral pain syndrome patients: a systematic review. *Braz J Phys Ther* 2015;19(3):167-76.

54. Bennell KL, Hunt MA, Wrigley TV, et al. The effects of hip muscle strengthening on knee load, pain, and function in people with knee osteoarthritis: a protocol for a randomised, single-blind controlled trial. *BMC Musculoskelet Disord* 2007;8:121.

55. Lorimer AV, Hume PA. Achilles tendon injury risk factors associated with running. *Sports Med* 2014;44(10):1459-72.

56. Silbernagel KG, Thomeé R, Eriksson BI, et al. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med* 2007;41(4):276-80.

57. O'Neill S, Barry S, Watson P. Plantarflexor strength and endurance deficits associated with mid-portion Achilles tendinopathy: The role of soleus. *Phys Ther Sport* 2019;37:69-76.

58. Kulig K, Loudon J, Popovich J, et al. Dancers with Achilles tendinopathy demonstrate altered lower extremity takeoff kinematics. *J Orthop Sports Phys Ther* 2011;41(8):606-13.

59. Silbernagel KG, Gustavsson A, Thomeé R, et al. Evaluation of lower leg function in patients with Achilles tendinopathy. *Knee Surg Sports Traumatol Arthrosc* 2006;14(11):1207-17.

60. Claudino JG, Cronin J, Mezencio B, et al. The countermovement jump to monitor neuromuscular status: A meta-analysis. *J Sci Med Sport* 2017;20(4):397-402.

61. Sancho I, Morrissey D, Willy RW, et al. Education and exercise supplemented by a pain-guided hopping intervention for male recreational runners with midportion Achilles tendinopathy: A single cohort feasibility study. *Phys Ther Sport* 2019;40:107-16.

62. Tijssen M, van Cingel R, de Visser E, et al. A clinical observational study on patient-reported outcomes, hip functional performance and return to sports activities in hip arthroscopy patients. *Phys Ther Sport* 2016;20:45-55.

63. Moore D, Semciw AI, Pizzari T. A systematic review and meta-analysis of common therapeutic exercises that generate highest muscle activity in the gluteus medius and gluteus minimus segments. *Int J Sports Phys Ther* 2020;15(6):856-81.

64. Moore D, Pizzari T, McClelland J, et al. Rehabilitation Exercises for the Gluteus Medius Muscle Segments: An Electromyography Study. *J Sport Rehabil* 2019;28(8):jsr.2018-0340.

65. Kountouris A, Cook J. Rehabilitation of Achilles and patellar tendinopathies. *Best Pract Res Clin Rheumatol* 2007;21(2):295-316.

66. Gajhede-Knudsen M, Ekstrand J, Magnusson H, et al. Recurrence of Achilles tendon injuries in elite male football players is more common after early return to play: an 11-year follow-up of the UEFA Champions League injury study. *Br J Sports Med* 2013;47(12):763-68.

67. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016;50(14):853-64.

68. van der Horst N, Backx F, Goedhart EA, et al. Return to play after hamstring injuries in football (soccer): a worldwide Delphi procedure regarding definition, medical criteria and decision-making. *Br J Sports Med* 2017;51(22):1583-91.

69. Verhagen AP, de Vet HC, de Bie RA, et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998;51(12):1235-41.

70. Murphy MK, Black NA, Lamping DL, et al. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998;2(3):i-iv, 1-88.

71. Shrier I. Strategic Assessment of Risk and Risk Tolerance (StARRT) framework for return-to-play decision-making. *Br J Sports Med* 2015;49(20):1311-5.

72. Vicenzino B, de Vos RJ, Alfredson H, et al. ICON 2019-International Scientific Tendinopathy Symposium Consensus: There are nine core health-related domains for tendinopathy (CORE DOMAINS): Delphi study of healthcare professionals and patients. *Br J Sports Med* 2020;54(8):444-51.

73. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001;35(5):335-41.

74. Murphy M, Rio E, Debenham J, et al. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: a review of outcome measures for self- reported pain and function. *Int J Sports Phys Ther* 2018;13(2):283-92.

75. Iversen JV, Bartels EM, Langberg H. The Victorian Institute of Sports Assessment - Achilles questionnaire (VISA-A) - a reliable tool for measuring Achilles tendinopathy. *Int J Sports Phys Ther* 2012;7(1):76-84.

76. Mc Auliffe S, Synott A, Casey H, et al. Beyond the tendon: Experiences and perceptions of people with persistent Achilles tendinopathy. *Musculoskelet Sci Pract* 2017;29:108-14.

77. Turner J, Malliaras P, Goulis J, et al. "It's disappointing and it's pretty frustrating, because it feels like it's something that will never go away." A qualitative study exploring individuals' beliefs and experiences of Achilles tendinopathy. *PLoS One* 2020;15(5):e0233459.

APPENDICES

Summary

Nederlandse samenvatting

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SUMMARY

Midportion Achilles tendinopathy is one of the most prevalent overuse injuries of the lower extremity, with the highest incidence reported in athletes who participate in sports involving running and/or jumping. Symptoms can persist for years and may result in severe limitations of sports participation. Whilst knowledge on pathophysiology and aetiology has increased, these areas still need to be further elucidated. As a consequence, many different treatment options have emerged, but treatment often remains a challenge.
The aim of this thesis was to enlarge the evidence base on conservative treatment of midportion Achilles tendinopathy. More specifically, the studies reported in this thesis aimed to investigate the most effective loading programme, explore the potential role of hip muscle dysfunction and investigate the definition of, and criteria for return to sport (RTS).
In **Chapter 1**, we provide an overview of the current knowledge regarding anatomy, pathophysiology, risk factors and different treatment options for midportion Achilles tendinopathy.

During the last decades, there has been an increasing interest in the use of loading interventions for midportion Achilles tendinopathy, with a strong bias towards eccentric loading. Despite the common beneficial effects of this intervention, the optimum dosage remained unclear. In **Chapter 2**, we performed a systematic literature review. Several electronic databases were explored to identity the most effective eccentric loading protocol and to describe the associated training parameters. The Physiotherapy Evidence Database (PEDro) score was used to assess methodological quality of the included studies and to interpret the level of evidence. Based on 14 randomized and clinical controlled trials, strong evidence was found for the original Alfredson programme, in which eccentric heel-lowering exercises are performed at slow pace, for 3 sets of 15 repetitions, twice daily, and both with a straight and bent knee. Strong evidence was also found for a gradual onset of exercises during the first week of the Alfredson programme, but no specific protocol could be recommended. Additionally, our results showed that other eccentric loading protocols may achieve similar results, but many studies showed methodological limitations or lacked a detailed description of their training parameters. Therefore, no definitive conclusion could be made regarding the most effective training parameters.

Whilst eccentric loading became the mainstay of treatment for midportion Achilles tendinopathy, the rationale for isolating the eccentric phase remained controversial. Consequently, loading programmes using different contraction modes, such as the Silbernagel combined concentric-eccentric loading programme, have emerged. To compare the effectiveness of the Alfredson programme with the Silbernagel programme, the design of a randomised controlled trial was set out in **Chapter 3** (study protocol). Recreational athletes, 18-65 years of age, with chronic unilateral tendinopathy 2-7 cm above the Achilles insertion were included. They were randomised into two groups performing either 12 weeks of home-based loading exercises according to the Alfredson or according to the Silbernagel programme. The primary outcome measure was the Victorian Institute of Sports Assessment – Achilles (VISA-A) at one-year follow-up. Secondary outcome measures were visual analogue scores for pain during daily activities (VAS-ADL) and sport (VAS-sport), quality of life (EQ-5D), and global perceived effect. Furthermore, several functional outcome measures were assessed. Plantar flexor endurance was assessed with the heel-raise test, jump height was assessed using the single-leg countermovement jump, and we evaluated hip muscle strength with a handheld dynamometer. Furthermore, the RTS rate was evaluated. Measurements were performed at baseline, and at 12 weeks, 26 weeks and one-year follow-up. Analysis was performed using a linear mixed model analysis including intervention (Alfredson group as reference), time and intervention by time-interaction, and with adjustment for baseline values and confounders (i.e. gender, age and duration of symptoms).

Chapter 4 focuses on the clinical outcomes. A total of 40 recreational athletes were randomised into the Alfredson group (n = 18) and the Silbernagel group (n = 22). Mean VISA-A score significantly improved in both the Alfredson group (60.7±17.1 to 89.4±13.0) and the Silbernagel group (59.8±22.2 to 83.2±22.4), but after correction for baseline VISA-A score and confounders, no significant difference between the groups was found (2.4, 95% CI [-8.5, 13.3], $P = 0.656$). Pain scores also significantly improved within both groups (VAS-ADL: 28.6±22.1 to 5.8±8.3 in the Alfredson group, and 28.6±31.8 to 9.0±23.0 in the Silbernagel group; VAS-sport: 44.8±26.8 to 13.1±20.2 in the Alfredson group, and 46.6±32.6 to 12.8±24.6 in the Silbernagel group). Yet, after adjustment for the respective baseline values and confounders, no significant differences were found between the groups (VAS-ADL: -2.0, 95% CI [-11.3, 7.3], $P = 0.665$, and VAS-sport: 1.3, 95% CI [-12.8, 15.3], $P = 0.858$). Subscales of the EQ-5D improved in both groups, but in the Silbernagel group, significantly more participants considered themselves improved at one-year follow-up (77% versus 50%). We found that both programmes showed rather high adherence rates (Alfredson group: 74%, Silbernagel group: 77%), indicating that intensive supervision by a health professional may not be necessary.

Chapter 5 focuses on functional outcomes. At one-year follow-up, we found significant improvement of plantar flexor endurance and hip external rotator strength of the injured limb in both groups, but after correction for baseline values and confounders, no significant differences were detected between the groups (heel-raise test: 2.7, 95% CI [-0.5, 5.9], $P = 0.092$, hip external rotator strength: -0.1, 95% CI [-0.2, 0.0], $P = 0.193$). Regarding jump height and strength of the hip abductors and extensors, we found no significant improvement within both groups, and also, after correction for baseline values and confounders, no significant differences between the groups were found. The RTS rate at one-year follow-up was 80% higher in the group that performed the Silbernagel programme.
It was concluded that both the Alfredson and Silbernagel programme yield significant improvement in clinical symptoms and functional performance during the one-year follow-up period, and that these effects tend to be similar between both programmes. Given

the beneficial effects and high adherence rates, both programmes are considered an effective treatment strategy for mid-portion Achilles tendinopathy. Based on these findings, the relevance of contraction mode in rehabilitation of Achilles tendinopathy may be questioned.

In line with other loading programmes, the Alfredson and Silbernagel programme merely involve plantar flexor strengthening exercises, whilst functional performance of the entire lower extremity may be affected. In the cross-sectional study presented in **Chapter 6**, we aimed to investigate whether recreational athletes with unilateral midportion Achilles tendinopathy demonstrate strength differences in the proximal hip muscle groups compared with asymptomatic controls, who were matched on age, sport type and current training extent. In a sample of 12 athletes, we performed isometric strength measurements of the hip abductors, extensors and external rotators using a handheld dynamometer, and we evaluated the single leg squat for functional performance of the hip muscle groups. Additionally, participants completed the VISA-A questionnaire to record the severity of their symptoms. Compared with the control group, the Achilles tendinopathy group demonstrated significantly less isometric hip abduction (29%), hip extension (28%), and hip external rotation strength (34%) in their injured limb. Similar differences were found for the non-injured limb (27% to 42%). No significant differences were found in functional hip muscle performance between the injured and non-injured limb or between the Achilles tendinopathy and the control group. Furthermore, the diminished hip muscle strength was not significantly correlated with the VISA-A score.
Although the cross-sectional nature of the study impedes from drawing a firm conclusion, these findings illustrate that pronounced bilateral strength deficits of the proximal hip muscle groups may be present in athletes with unilateral midportion Achilles tendinopathy.

The ultimate rehabilitation goal of athletes with midportion Achilles tendinopathy is to resume their sports activities as quickly as possible. However, it remains unclear how successful RTS should be defined and which criteria should be used for the RTS decision-making. In the qualitative systematic review described in **Chapter 7**, we aimed to systematically synthesize the available literature for definitions of, and criteria for RTS. A qualitative content analysis was used to analyze the included studies and extract relevant definitions and criteria. Thirty-five studies were included in the content analysis, showing large variety in both the definitions and criteria. The main themes for defining successful RTS after midportion Achilles tendinopathy were 'reaching pre-injury activity/sports level, with the ability to perform training and matches without limitations', 'absence of pain' and 'recovery'. Regarding criteria for RTS, 'level of pain', 'level of functional recovery', 'recovery of muscle strength', 'recovery of range of motion', 'level of endurance of the involved limb', 'medical advice', 'psychosocial factors', and 'anatomical/physiological properties of the musculotendinous complex' were identified as the main themes. Unfortunately, the literature lacked specific outcome measures and well-defined cut-off values.

In conclusion, this systematic review showed that, in the current scientific literature, RTS after midportion Achilles tendinopathy is defined according to the pre-injury level of sports (including both training and matches), but also with terms related to the absence of pain and recovery. However, based on the findings of this review, no definitive conclusion could be made regarding either an unambiguous definition of RTS or a set of validated outcome measures. Therefore, further research on this topic is definitely needed.

In **Chapter 8** the main findings of this thesis are put in a broader perspective, and we reflect on the results and limitations of our studies. Implications for clinical practice are provided, and recommendations are made for future research. New studies on midportion Achilles tendinopathy should investigate the relevance of various training parameters within loading programmes, and explore the underlying mechanisms of action. Additionally, consensus should be reached on determinants that need to be considered when selecting an appropriate loading intervention. The potential relation between midportion Achilles tendinopathy and decreased functional performance of the lower extremity should be further explored, and results may be implemented in rehabilitation as well as in prevention programmes. Lastly, studies to reach consensus on an unambiguous definition of RTS and on a set of validated outcome measures to assist in RTS decision making should be conducted. This future research should enhance the effectiveness of rehabilitation of athletes with midportion Achilles tendinopathy.

APPENDICES

NEDERLANDSE SAMENVATTING
(Summary in Dutch)

Midportion achilles tendinopathie is één van de meest voorkomende overbelastingsletsels van de onderste extremiteit. De hoogste incidentie wordt gerapporteerd bij hardlopen en sprongsporten. De blessure kan gepaard gaan met langdurige klachten en kan leiden tot grote problemen in sportparticipatie. Ondanks een toename van kennis over de pathofysiologie en etiologie van midportion achilles tendinopathie, is er nog steeds veel onduidelijk. Het gevolg hiervan is dat er in de laatste decennia verschillende behandelvormen zijn ontwikkeld. Desondanks blijft het inzetten van de meest optimale behandeling van achilles tendinopathie nog steeds een uitdaging voor zorgverleners.
Het overkoepelende doel van dit proefschrift was het vergroten van de kennis over conservatieve behandeling van midportion achilles tendinopathie. Specifieke doelstellingen van de studies in dit proefschrift waren het onderzoek naar het meest effectieve oefenprogramma en naar een mogelijke betrokkenheid van verminderde functie van de heupmusculatuur bij deze aandoening. Daarnaast werd bestudeerd hoe, op basis van de wetenschappelijke literatuur, terugkeer naar sport wordt gedefinieerd en welke criteria daarvoor worden gebruikt. **Hoofdstuk 1** geeft een overzicht van de anatomie, pathofysiologie, risicofactoren en verschillende behandelvormen voor midportion achilles tendinopathie.

De laatste decennia is midportion achilles tendinopathie veelvuldig behandeld met oefentherapie. De voorkeur ging daarbij duidelijk uit naar excentrische oefentherapie. Ondanks het feit dat excentrische oefentherapie over het algemeen positieve effecten liet zien, bleef het onduidelijk wat het meest optimale protocol was.
In **Hoofdstuk 2** wordt een systematisch literatuuronderzoek beschreven. Verschillende elektronische databases werden doorzocht naar het meest effectieve protocol voor excentrische oefentherapie en de meest effectieve trainingsparameters. Om de methodologische kwaliteit van de geïncludeerde studies te bepalen en de bewijskracht vast te stellen werd de Physiotherapy Evidence Database (PEDro) score gebruikt. Gebaseerd op 14 geïncludeerde gerandomiseerde en quasi-gerandomiseerde studies werd sterke bewijskracht gevonden voor het originele excentrische oefenprogramma zoals beschreven door Alfredson. Dit programma bestaat uit langzaam uitgevoerde excentrische kuitoefeningen, welke tweemaal per dag worden uitgevoerd voor 3 series van 15 herhalingen, met zowel een gestrekte als gebogen knie. Er werd ook sterke bewijskracht gevonden voor een graduele opbouw van de excentrische kuitoefeningen gedurende de eerste week van het Alfredson programma, maar er kon geen aanbeveling worden gedaan voor een specifiek protocol. De resultaten toonden daarnaast aan dat andere programma's mogelijk even effectief zijn. Echter, de geïncludeerde studies waren van matige methodologische kwaliteit en gedetailleerde beschrijvingen van de trainingsparameters ontbraken. Dientengevolge kon geen conclusie worden getrokken met betrekking tot de meest effectieve trainingsparameters voor excentrische oefentherapie bij midportion achilles tendinopathie.

Hoewel excentrische oefentherapie werd gezien als de gouden standaard voor behandeling van midportion achilles tendinopathie, bleef de gedachte om te kiezen voor enkel de excentrische component controversieel. Hierdoor maakten oefenprogramma's zoals het programma van Silbernagel, dat bestaat uit zowel concentrische als excentrische oefeningen, hun opwachting. Teneinde de effectiviteit van het Alfredson en het Silbernagel programma te vergelijken, werd een gerandomiseerd gecontroleerd klinisch onderzoek uitgevoerd. De opzet van deze gerandomiseerde studie is beschreven in **Hoofdstuk 3** (studie protocol). Recreatieve sporters tussen de 18 en 65 jaar, met een chronische unilaterale tendinopathie 2-7 cm boven de insertie van de achillespees op de calcaneus werden geïncludeerd. Zij werden verdeeld over 2 groepen, die gedurende 12 weken thuis het oefenprogramma van Alfredson of Silbernagel uitvoerden. De primaire uitkomstmaat was de Victorian Institute of Sports Assessment – Achilles (VISA-A) vragenlijst na 1 jaar follow-up. Secundaire uitkomstmaten waren visueel analoge pijnscores tijdens dagelijkse activiteiten (VAS-ADL) en tijdens sport (VAS-sport), kwaliteit van leven (EQ-5D) en de globaal ervaren effectscore. Daarnaast werden verschillende functionele uitkomstmaten gemeten. Het krachtuithoudingsvermogen van de plantairflexoren werd geëvalueerd met de heel-raise test, de éénbenige countermovement jump werd gebruikt voor het meten van spronghoogte, en kracht van de heupmusculatuur werd gemeten met behulp van een handheld dynamometer. Daarnaast werd terugkeer naar sport geëvalueerd. Metingen werden uitgevoerd op baseline, en na 12 weken, 26 weken en 1 jaar follow-up. Analyses werden uitgevoerd door middel van een linear mixed model analyse, met interventie (Alfredson groep als referentie), tijd en de interactie tussen interventie en tijd. Er werd gecorrigeerd voor baseline waarden en confounders (geslacht, leeftijd en duur van de symptomen).

De resultaten van de klinische uitkomstmaten zijn beschreven in **Hoofdstuk 4**. In totaal werden 40 recreatieve sporters gerandomiseerd, verdeeld over de Alfredson groep (n = 18) en de Silbernagel groep (n = 22). De VISA-A score toonde een significante verbetering in zowel de Alfredson groep (van 60,7±17,1 naar 89,4±13,0) als de Silbernagel groep (van 59,8±22,2 naar 83,2±22,4). Echter, na correctie voor baseline scores en confounders werd er geen significant verschil tussen beide groepen gevonden (2,4; 95% BHI [-8,5; 13,3], P = 0,656). Pijnscores verbeterden ook significant in beide groepen (VAS-ADL: van 28,6±22,1 naar 5,8±8,3 in de Alfredson groep, en van 28,6±31,8 naar 9,0±23,0 in de Silbernagel groep; VAS-sport: van 44,8±26,8 naar 13,1±20,2 in de Alfredson groep, en van 46,6±32,6 naar 12,8±24,6 in de Silbernagel groep). Echter, na correctie voor de respectievelijke baseline waarden en confounders, werden geen significante verschillen gevonden tussen de groepen (VAS-ADL: -2,0; 95% BHI [-11,3; 7,3], P = 0,665, and VAS-sport: 1,3; 95% BHI [-12,8; 15,3], P = 0,858). De subschalen van de EQ-5D verbeterden in beide groepen, maar significant meer deelnemers uit de Silbernagel groep ervaarden verbetering na 1 jaar follow-up (77% tegenover 50%). De adherentie voor beide oefenprogramma's was hoog (Alfredson groep: 74%, Silbernagel groep: 77%), hetgeen suggereert dat intensieve begeleiding door een zorgprofessional mogelijk niet strikt noodzakelijk is.

In **Hoofdstuk 5** worden de resultaten met betrekking tot de functionele uitkomstmaten beschreven. Na 1 jaar follow-up werd in het aangedane been zowel een significante toename van het krachtuithoudingsvermogen van de plantairflexoren als van de kracht van de exorotatoren van de heup gevonden in beide groepen. Echter, na correctie voor baseline waarden en confounders, was er geen sprake van een significant verschil tussen de twee groepen (heel-raise test: 2,7 herhalingen; 95% BHI [-0,5; 5,9], $P = 0,092$, kracht van de exorotatoren: -0,1 N/kg; 95% BHI [-0,2; 0,0], $P = 0,193$). De spronghoogte en kracht van de abductoren en extensoren van de heup toonden geen significante verbeteringen in beide groepen. Na correctie voor baseline waarden en confounders was er eveneens geen sprake van een significant verschil tussen beide groepen. Het percentage terugkeer naar sport bleek na 1 jaar follow-up in de Silbernagel groep 80% hoger dan in de Alfredson groep.
Op basis van deze gerandomiseerde gecontroleerde studie werd geconcludeerd dat oefentherapie uitgevoerd volgens het Alfredson- dan wel volgens het Silbernagel programma, beide resulteren in significante verbeteringen van klinische symptomen en functionele uitkomstmaten tot 1 jaar follow-up. De effecten lijken gelijk te zijn voor beide programma's. Gegeven deze gunstige effecten en de hoge adherentie kunnen beide programma's beschouwd worden als een effectieve interventie voor de behandeling van midportion achilles tendinopathie. Gebaseerd op deze bevindingen kan het belang van het type contractie in de revalidatie van achilles tendinopathie in twijfel worden getrokken.

In overeenstemming met andere programma's bestaan zowel het Alfredson- als het Silbernagel programma enkel uit oefeningen voor de plantairflexoren, hoewel bij midportion achilles tendinopathie de functie van de gehele onderste extremiteit kan zijn aangedaan. Derhalve was het doel van de cross-sectionele studie zoals beschreven in **Hoofdstuk 6** om de krachtsverschillen in de proximale heupmusculatuur te bestuderen tussen recreatieve sporters met een unilaterale midportion achilles tendinopathie en asymptomatische controle proefpersonen, die werden gematcht op leeftijd, type sport en huidige trainingsomvang. In een steekproef van 12 sporters werden isometrische krachttests van de abductoren, extensoren en exorotatoren van de heup uitgevoerd met behulp van een handheld dynamometer. Tevens voerden proefpersonen de éénbenige squat uit als een meer functionele prestatietest van de heupmusculatuur. Deelnemers vulden daarnaast de VISA-A vragenlijst in om de ernst van hun symptomen te meten. In vergelijking met de controlegroep hadden deelnemers met achilles tendinopathie significant minder kracht in hun heupabductoren (29%), -extensoren (28%) en -exorotatoren (34%) in hun aangedane zijde. Vergelijkbare verschillen werden gevonden voor de niet-aangedane zijde (27-42%). Er werden geen significante verschillen gevonden in de uitvoering van de éénbenige squat, noch tussen de aangedane en niet-aangedane zijde, noch tussen de deelnemers met achilles tendinopathie en de controlegroep. Bovendien bleek er geen significante correlatie tussen de verminderde heupspierkracht en de VISA-A score te bestaan.
Hoewel op basis van het cross-sectionele design geen harde conclusies kunnen worden getrokken, laten deze bevindingen zien dat sporters met een unilaterale midportion achilles tendinopathie forse krachtsvermindering van hun heupmusculatuur kunnen hebben

in zowel de aangedane als niet-aangedane zijde.
Het ultieme doel van sporters met een achilles tendinopathie is het zo snel mogelijk hervatten van hun sportactiviteiten. Desondanks blijft het onduidelijk hoe succesvolle terugkeer naar sport moet worden gedefinieerd en welke criteria moeten worden gebruikt om de besluitvorming rondom terugkeer naar sport te ondersteunen. De kwalitatieve systematische literatuurstudie beschreven in **Hoofdstuk 7** had als doel om op systematische wijze binnen de beschikbare wetenschappelijke literatuur te zoeken naar definities van terugkeer naar sport en criteria die werden gebruikt voor de besluitvorming rondom terugkeer naar sport. De geïncludeerde studies werden geanalyseerd met behulp van een content analyse, waarbij relevante definities en criteria werden geëxtraheerd. In totaal werden 35 studies geïncludeerd in deze content analyse. Deze studies lieten een grote variatie zien in zowel de gebruikte definities als criteria. De belangrijkste thema's voor het definiëren van terugkeer naar sport na midportion achilles tendinopathie waren 'het bereiken van het sport-/activiteitenniveau van vóór de blessure, met de mogelijkheid om zonder beperkingen deel te nemen aan trainingen en wedstrijden', 'afwezigheid van pijn' en 'herstel'. Met betrekking tot criteria voor het ondersteunen van de besluitvorming rondom terugkeer naar sport bleken 'pijnniveau', niveau van functioneel herstel', 'herstel van spierkracht', herstel van range of motion', 'uithoudingsvermogen van het aangedane been', 'medisch advies', psychosociale factoren' en 'anatomische/fysiologische eigenschappen van het spier-pees-complex' de belangrijkste thema's. Helaas werden in de geïncludeerde studies geen specifieke uitkomstmaten en concrete afkapwaarden geformuleerd.
Samengevat toonde dit systematische literatuuronderzoek aan dat, binnen de huidige wetenschappelijke literatuur, terugkeer naar sport na midportion achilles tendinopathie wordt gedefinieerd in termen van het sportniveau van vóór de blessure (zowel met betrekking tot trainingen als wedstrijden). Aspecten gerelateerd aan de afwezigheid van pijn en herstel werden tevens gebruikt voor de definitie. Echter, op basis van de bevindingen van dit literatuuronderzoek kon geen ondubbelzinnige definitie worden gegeven van terugkeer naar sport na een midportion achilles tendinopathie, noch kon een set van gevalideerde uitkomstmaten worden opgesteld. Daarom is verder onderzoek naar dit onderwerp noodzakelijk.

In **Hoofdstuk 8** worden de belangrijkste bevindingen van dit proefschrift in een breder perspectief geplaatst en wordt gereflecteerd op de resultaten en beperkingen van de uitgevoerde studies. Daarnaast worden praktische implicaties besproken en aanbevelingen voor toekomstig onderzoek gedaan. Toekomstige studies naar midportion achilles tendinopathie zullen zich moeten richten op het onderzoeken van verschillende trainingsparameters van oefenprogramma's en het bestuderen van onderliggende werkingsmechanismen hieromtrent. Daarnaast zou consensus met betrekking tot aspecten die moeten worden overwogen bij het selecteren van een passend oefenprogramma de behandeling van deze blessure positief kunnen beïnvloeden. De potentiële relatie tussen midportion achilles tendinopathie en verminderde functionele prestaties van de onderste extremiteit dienen verder te worden onderzocht, en de resultaten van dit onderzoek kunnen

vervolgens worden geïmplementeerd in zowel revalidatie- als in preventieprogramma's. Tot slot zouden studies zich moeten toeleggen op het bereiken van consensus omtrent een ondubbelzinnige definitie van terugkeer naar sport na een midportion achilles tendinopathie en over een set gevalideerde uitkomstmaten die gebruikt kunnen worden bij de besluitvorming rondom terugkeer naar sport. Met deze toekomstige studies zal de effectiviteit van de revalidatie van sporters met midportion achilles tendinopathie verder kunnen worden verbeterd.

APPENDICES

DANKWOORD

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APPENDICES

ABOUT THE AUTHOR

Curriculum vitae

Bas Habets was born on March 18, 1982 in Deurne. He spent his childhood in and around Asten. He obtained his pre-university degree at Varendonck College in Asten in 2000, and in the same year he moved to Utrecht to study Physiotherapy at Utrecht University of Applied Sciences. After finishing this study, he started working as a physiotherapist at Papendal Sports Medical Center, with a focus on musculoskeletal rehabilitation of (elite) athletes.
In 2010 he obtained a master's degree in Orthopedic Manual Therapy at Utrecht University of Applied Sciences, and in 2014 he obtained a master's degree (with honor) in Clinical Health Sciences, Physiotherapy Science at Utrecht University. During the latter study, he started studying Achilles tendinopathy for the purpose of the development of a tendon clinic at Papendal Sports Medical Center. As of March 2015, he was given the opportunity by prof. dr. Frank Backx to continue his research in a PhD project at the Department of Rehabilitation, Physical Therapy Science & Sports at Utrecht University Medical Center.
During his PhD project, he ended his career as physiotherapist and started working for ONVZ Health Insurer. From 2018-2021, he worked as policy advisor and corporate health manager, advising various corporates on sustainable employability for their employees. Since April 2021, he works as consultant/project manager for Allegro Medical, supervising different projects on e-health and digital transformation in healthcare.

PhD portfolio summary

Name PhD student:	Bas Habets
Institute:	University Medical Center Utrecht Department of Rehabilitation, Physical Therapy Science & Sports
PhD period:	01.03.2015 – 18.11.2021
Promotor:	Prof. dr. F.J.G. Backx
Supervisors:	Dr. B.M.A. Huisstede, Dr. R.E.H. van Cingel

PhD training

Courses

Online English academic writing, University of Amsterdam	2014
Basiscursus Regelgeving en Organisatie voor Klinisch Onderzoekers (BROK), Nederlandse Federatie van Universitair Medische Centra (NFU)	2017
Research data management, Utrecht University	2017

(Inter)national conferences – attendance

Symposium "Treatment of tendinopathy", Groningen	2015
Annual congress of the Dutch Sports Medicine Society, Ermelo and Eindhoven (5x)	2015-2019

(Inter)national conferences – presentations

Midportion Achilles tendinopathy is associated with decreased hip muscle strength in male athletes: a cross-sectional study. Annual congress of the Dutch Sports Medicine Society, Ermelo	2015
Rehabilitation after Achilles tendon rupture. Annual congress of the Dutch Sports Medicine Society, Ermelo	2015
Eccentric training in chronic midportion Achilles tendinopathy: a systematic review on different protocols. Annual congress of the Dutch Sports Medicine Society, Ermelo	2016
High-energy ankle trauma. Symposium MarkTwo Academy, Zeist	2017
Return to sport in athletes with midportion Achilles tendinopathy: a qualitative systematic review regarding definitions and criteria. Annual congress of the Dutch Sports Medicine Society, Ermelo	2017
Rehabilitation of Achilles tendinopathy. Symposium Ankle and foot injuries, Arnhem	2017

Chronic Achilles tendon injuries. Post-academic education for general practitioners, Zeist	2017
Return to sport in athletes with midportion Achilles tendinopathy. Barça Sports Medicine Conference, Barcelona	2018

Teaching

Lecturer at Master Musculoskeletal Rehabilitation, HAN University of Applied Sciences, Nijmegen	2016-2017

Other activities

Reviewer for (inter)national journals: *Scandinavian Journal of Medicine and Science in Sports* *Sport & Geneeskunde* *JSM Foot & Ankle* *Disability and Rehabilitation*	2015-2018

List of publications

International peer-reviewed publications

Habets B, Van Cingel REH. Eccentric exercise training in chronic mid-portion Achilles tendinopathy: a systematic review on different protocols. *Scand J Med Sci Sports* 2015;25(1):3-15.

Thorborg K, Tijssen M, **Habets B**, Bartels EM, Roos EM, Kemp J, Crossley KM, Hölmich P. Patient-reported outcome (PRO) questionnaires for young-aged to middle-aged adults with hip and groin disability: a systematic review of the clinimetric evidence. *Br J Sports Med* 2015;49(12):812.

Habets B, Van Cingel REH, Ostelo RJWG. Reproducibility of a battery of commonly used clinical tests to evaluate lumbopelvic motor control. *Phys Ther Sport* 2015 Nov;16(4):331-9.

Slade S, Dionne C, Underwood M, Buchbinder R, Beck B, Bennell K, Brosseau L, Costa L, Cramp F, Cup E, Feehan L, Ferreira M, Forbes S, Glasziou P, **Habets B**, Harris S, Hay-Smith J, Hillier S, Hinman R, Holland A, Hondras M, Kelly G, Kent P, Lauret G, Long A, Maher C, Morso L, Osteras N, Peterson T, Quinlivan R, Rees K, Regnaux JP, Rietberg M, Saunders D, Skoetz N, Sogaard K, Takken T, Van Tulder M, Voet N, Ward L, White C. Consensus on Exercise Reporting Template (CERT): modified Delphi study. P*hys Ther* 2016;96(10):1514-24.

Dejaco B, **Habets B**, Van Loon CJM, Van Grinsven S, Van Cingel REH. Eccentric versus conventional exercise therapy in patients with rotator cuff tendinopathy: a randomized single blinded controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2017;25(7):2051-2059.

Habets B, Smits HW, Backx FJG, Van Cingel REH, Huisstede BMA. Hip muscle strength is decreased in middle-aged recreational athletes with midportion Achilles tendinopathy. *Phys Ther Sport* 2017;25:55-61.

Van Cingel R, **Habets B**, Willemsen L, Staal B. Shoulder dynamic control ratio and rotation range of motion in female junior elite handball players and controls. *Clin J Sports Med* 2018;28(2):153.158.

Van Lankveld W, Van Melick N, **Habets B**, Roelofsen E, Staal B, Van Cingel R. Measuring individual hierarchy of anxiety invoking sports related activities: development and validation of the Photographic Series of Sports Activities for Anterior Cruciate Ligament Reconstruction (PHOSA-ACLR). *BMC Musculoskelet Disord* 2017;18:287.

Habets B, Van Cingel REH, Backx FJG, Huisstede BMA. Alfredson versus Silbernagel exercise therapy in chronic midportion Achilles tendinopathy: study protocol for a randomized controlled trial. *BMC Musculoskelet Disord* 2017;18:296.

Habets B, Van den Broek A, Huisstede BMA, Backx FJG, Van Cingel REH. Return to sport in athletes with midportion Achilles tendinopathy: A qualitative systematic review regarding definitions and criteria. *Sports Med* 2017;48(3):705-723.

Habets B, Staal JB, Tijssen M, Van Cingel R. Intrarater reliability of the Humac NORM isokinetic dynamometer for strength measurements of the knee and shoulder muscles. *BMC Res Notes* 2018;11:15.

Lankveld W, Van Melick N, **Habets B**, Pronk Y, Staal JB, Van Cingel R. Dutch Knee Self Efficacy Scale: cross-cultural adaptation, measurement properties and a proposed alternative scoring system based on Confirmatory Factor Analysis. *BMC Sports Sci Med Rehabil* 2019;11:3.

Habets B, Van Cingel REH, Backx FJG, Van Elten HJ, Zuithoff NPA, Huisstede BMA. No difference in clinical effects when comparing Alfredson eccentric and Silbernagel combined concentric-eccentric loading in Achilles tendinopathy: A randomized controlled trial. *Orthop J Sports Med*; accepted June 2021

Habets B, Huisstede BMA, Backx FJG, Van Elten HJ, Zuithoff NPA, Van Cingel REH. Alfredson versus Silbernagel loading programme in recreational athletes with midportion Achilles tendinopathy: A randomized controlled trial comparing functional performance of the lower extremity and return to sport. Under review

National peer-reviewed publications

Habets B, Van Cingel REH. Rompstabiliteit meten: praktische consequenties voor de fysiotherapeut. *Physios* 2011;2:12-20.

Ilbrink S, Kokshoorn APJ, Van Loon CJM, **Habets B**. Het fabella syndroom. *Sport & Geneeskunde* 2013;46(3): 20-24.

Ruitenbeek JJAC, **Habets B**. Oefentherapie gericht op motor control impairment bij lage rugklachten. *Physios* 2017;9(3):25-33.

Habets B, Huisstede B, Van Cingel R. Achillestendinopathie, Deel I: Anatomie, pathofysiologie, etiologie en epidemiologie. *Sportgericht* 2018;72(3):19-23.

Habets B, Van Cingel R, Huisstede B. Achillestendinopathie, Deel II: Diagnostiek en extra handvatten. *Sportgericht* 2018;72(5):20-23.

Habets B, Huisstede B, Van Cingel R. Achillestendinopathie, Deel III: Behandeling. *Sportgericht* 2019;73(1):100-105.

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