Achilles tendinopathy: new insights in cause of pain, diagnosis and management

van Sterkenburg, M.N.

Publication date
2012

Chapter 4

Less promising results with sclerosing Ethoxysclerol injections for midportion Achilles tendinopathy

A retrospective study

MN van Sterkenburg

MC de Jonge

IN Sierevelt

CN van Dijk

Am J Sports Med 2010; 38: 2226-2232

ABSTRACT

Background

In patients with complaints of chronic midportion Achilles tendinopathy, neovascularisation around the Achilles tendon and structural changes in the area were observed, but not in pain free normal tendons. Local injections of the sclerosing substance Polidocanol (Ethoxysclerol) have shown to yield good clinical results in patients with chronic Achilles tendinopathy. After training by the inventors of the technique, sclerosing Ethoxysclerol injections were applied on a group of patients in our center.

Hypothesis

We hypothesized that sclerosing Ethoxysclerol injections did not yield good results in the majority of patients.

Study design

Retrospective cohort study with 2.7-5.1 year follow-up.

Methods

In 113 patients (140 tendons) with midportion Achilles tendinopathy, 62 patients (70 tendons) showing neovascularisation on colour Doppler ultrasound (US) were identified. 53 Achilles tendons (48 patients) were treated with sclerosing Ethoxysclerol injections, with intervals of 6 weeks and a maximum of 5 sessions. Treatment was completed when neovascularisation or pain had disappeared, or when there was no positive treatment effect after 3-4 sessions.

Results

Fourty-eight patients (20 females and 28 males) with a median age of 45 (33-68) years, were treated. Median symptom duration was 23 months (range 3 to 300). Fifty-three tendons were treated with a median of 3 sessions of Ethoxysclerol injections. Six weeks after the last injection, 35% had no complaints, 9% minimal, 42% had the same and 14% had more complaints. Pain correlated positively with neovessels on US ($p<0.01$). At 2.7-5.1 year follow-up, 53% had received additional (surgical/ conservative) treatment, and 3 of these patients (7.5%) still had complaints of midportion Achilles tendinopathy. In 6 complaints after six weeks had resolved spontaneously.

Conclusion

Our study did not confirm the high beneficial value of sclerosing neovascularisation in patients with midportion Achilles tendinopathy.

Clinical Relevance

In recent years good results on the injection of sclerosing Ethoxysclerol have been reported, which we were not able to reproduce. Despite the retrospective design of our study, we consider it important to stress that injection of Ethoxysclerol may not be as promising as was thought.

INTRODUCTION

Chronic midportion Achilles tendinopathy is a common painful condition that is generally difficult to treat. It is defined as a painful thickening of the tendon typically 2-7 cm proximal to its insertion in the calcaneus, without an inflammatory cellular response inside the tendon[2]. Often it is accompanied by paratendinopathy. Complaints consist of long-term pain, tenderness and stiffness. The most apparent finding from clinical examination is a painful nodule on palpation of the Achilles tendon. On ultrasound (US) or Magnetic Resonance Imaging (MRI) examination thickening of the tendon and structural abnormalities in the painful area are seen.

Currently, a wide range of conservative treatments is available for midportion Achilles tendinopathy such as cast immobilisation, night splint, heel-raise, wait-and-see policy, friction therapy, shock-wave treatment, and eccentric training of the muscle-tendon complex[6,32,34,38,45].

Studies on eccentric training have generally showed good outcomes in the majority of patients[6,14,26,31,39,42]. Other studies have not been able to replicate these results[12,38]. When conservative measures fail surgical treatment is indicated. To reduce the necessity of surgical interference, new conservative measures have been developed worldwide. In 2002, a new type of injection therapy was introduced[30].

Using colour Doppler ultrasound, neovascularisation on the ventral side of the Achilles tendon was demonstrated in symptomatic patients[21]. Normal tendons lack these changes. It was hypothesized that neovessels and accompanying nerves were responsible for the pain in Achilles tendinopathy. Local injections of these areas with neovascularisation with Polidocanol (Ethoxysclerol) gave good clinical results in a double blind randomised controlled trial on patients with chronic Achilles tendinopathy[5,30]. At 2-year follow-up, they showed remaining good clinical results[25].

One of our radiologists specialized in musculoskeletal radiology, was trained by the inventors of the procedure to perform it according to the method as originally described[30]. From August 2004 until February 2007 48 patients were treated with Ethoxysclerol injections for chronic midportion Achilles tendinopathy. The purpose of this study was to analyze our results of this new intervention.

METHODS

Between August 2004 and February 2007, a total of 113 consecutive patients with 140 symptomatic Achilles tendons underwent colour Doppler ultrasonography investigation (US). Patients with midportion Achilles tendinopathy and neovascularisation were offered

treatment with Ethoxysclerol. Sixty-two patients had 70 symptomatic tendons showing neovascularisation (50%). In 50% of tendons with Achilles tendinopathy no neovessels were found. Fourteen patients were excluded from treatment because they refused sclerosing therapy (Figure 1). Results of these injections were retrospectively analyzed.

Ultrasonography and colour Doppler examination (US)

All tendons were examined with high-resolution greyscale ultrasound and with colour Doppler. A linear 17 MHz transducer was used. Achilles tendons showing midportion tendinopathy with neovascularisation, and accompanying clinical data concerning age, gender, symptom duration, presence and amount of neovascularisation, frequency of injections, and complaints after treatment were extracted.

Injection of Ethoxysclerol

Ethoxysclerol has a selective effect in the vascular intimae, causing thrombosis of the vessel, even if the injection is performed extravasally, which is important when very small vessels are targeted[16]. It also has a local anaesthetic effect.

Only patients, who already underwent six months of conservative treatment including physical therapy involving eccentric training for their current complaints, were offered this treatment.

If patients had at least a minimal amount of injectable neovascularisation (Figure 1) around their Achilles tendon on US, they were injected with Ethoxysclerol. Patients were in prone position, and the skin was washed with chlorohexidin 0.5% in 70% alcohol. For injection, a 23 gauge needle connected to a 3 ml syringe was used.

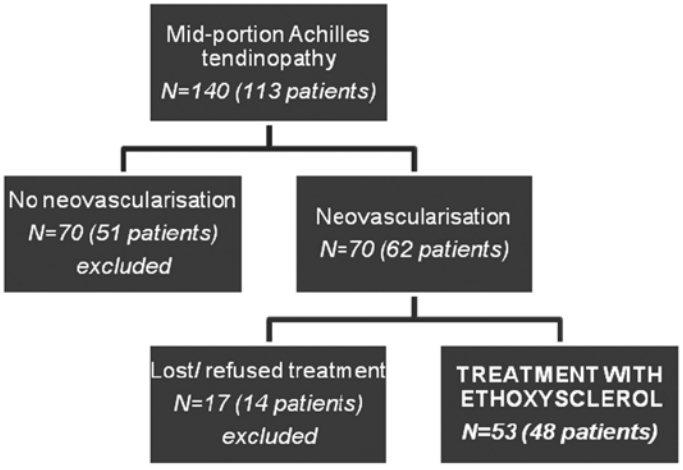

Figure 1. Number of tendons with neovascularisation and inclusion

The injections at the target vessels were performed under US guidance, from the medial side of the Achilles tendon to minimise the risk of sural nerve injury. Ethoxysclerol (2-4 ml) was injected until neovessels were no longer visible on US. After injection, a compressive bandage was applied. Patients were instructed to take the bandage off 24 hours after treatment, and free activity such as walking, bicycling, and light strength training were allowed the first 2 weeks. After these 2 weeks, free tendon loading activity was allowed.

Six weeks after treatment patients were assessed again by US, and if they still had complaints and neovascularisation injection with Ethoxysclerol was repeated, with a maximum of 5 treatments. Treatment was completed when no neovascularisation was present on US, when pain had disappeared, or when there was no positive treatment effect after 3 to 4 sessions. The same radiologist performed all US examinations and treatments.

Follow-up

The primary outcomes were defined as persistent pain and the absence or presence of neovascularisation. Patients were retrospectively questioned about the amount of pain six weeks after treatment as described on a 4- point scale as being no, minimal, same, or more. The amount of neovessels present after sclerosing therapy was described likewise as being no, minimal, same, or more by the radiologist performing the procedure. Information on weight, sports activity, employment, co- morbidity and medication was taken.

Subjective outcome at midterm follow-up (2.7-5.1 years; mean 3.9 years) was assessed using the same 4- point scale (no, minimal, same, or more), Visual Analogue Scales (VAS) for pain and function, and the Victorian Institute of Sports Assessment- Achilles (VISA-A) questionnaire. This questionnaire was created in 2001 to assess clinical severity for patients with Achilles tendinopathy. It is a self- administered questionnaire evaluating symptoms and their effect on physical activity[36]. Information was gathered on current sporting activity and interventions in the past years after sclerosing injections.

Statistical analysis

All obtained data were entered in a database and statistical analysis was performed using SPSS 15.0, (SPSS Inc., Chicago, IL, USA). Due to skewed distributions, continuous data (e.g. age, VAS, VISA-A) were described as medians and ranges and analysed non-parametrically. Categorical and dichotomous data (e.g. pain after treatment, complaints, amount of neovascularisation) were presented as frequencies and accompanying proportions. Wilcoxon Rank Sum test was performed to assess the change in sport activities/duration before and during complaints of the Achilles tendon, and to investigate change in pain level at six weeks and mid-term follow-up.

Spearman's correlation coefficient was calculated to determine the association between pain level and amount of neovessels at six weeks follow-up, and pain level and several demographic factors (symptom duration, age and BMI) at mid-term follow-up.

To assess whether gender significantly influenced complaints, we dichotomised complaints to none/minimal and same/more. Chi-square tests were performed and Odds- ratios (with 95%CI) were calculated. Mann Whitney U-tests were performed to assess difference in age between nine/minimal and same/more complaints and to assess a learning curve of the injection procedure. Therefore, we compared the dichotomised complaints six weeks after injection from the first and the last 15 patients.

Reported *P* values were 2-sided and were considered significant if p<.05.

RESULTS

Patient population

Demographics are summarized in table 1.

Table 1. Demographics

	Patients with Achilles tendinopathy	Patients with neovascularisation	Patients treated with sclerosing injections
Age (years) median (min-max)	46 (14-81)	47 (14-79)	45 (33-68)
Gender (m/f)	60 (53%)/53 (47%)	35 (56%)/27 (44%)	28 (70%)/20 (30%)
Side (l/r)	80 (57%)/60 (43%)	38 (54%)/32 (46%)	31 (58%)/22 (42%)

Forty-eight patients (53 tendons) were treated. Eleven patients (12 tendons) were lost to follow-up and one patient deceased. Thirty six patients (75%) with 40 treated tendons, 19 male and 17 female, with a median age of 50 (range; 38-72) and BMI of 25.9 (range; 21-39), returned the questionnaires for follow-up.

Median symptom duration before sclerosing was 23 months (range; 3-300). Five patients had comorbidity: cardiovascular symptoms (n=2), CRPS (n=1), fibromyalgia (n=1) and lipoedema of the legs (n=1). Nine patients used prescription drugs; of these 2 used inhalation glucocorticosteriods and the others used different medication for pain and cardiovascular disease.

Most subjects (58%) had fulltime employment in a physical or office setting. Prior to complaints, 30 out of the 36 patients (83%) were sports active. The most common activities were running (39%), tennis (22%) and soccer (14%). Sport level was recreational for 24 patients (67%), competitive for 11 patients (31%), and professional for 1 patient (2%). Median hours of sports activity a week was 4 (range; 0-30).

During complaints of midportion Achilles tendinopathy, 7 patients were unable to continue playing any sports and 1 voluntarily quit. Median number of hours a week playing sports diminished to 1 (range; 0-30) (p=0,00). Seven patients were still able to continue their activities on a competitive level.

The type of conservative treatment prior to sclerosing injections is shown in table 2.

Table 2. Most common types of conservative measures prior to injection with Ethoxysclerol

Conservative measures prior to sclerosing injections (n=46)	
Physical therapy (eccentric training, friction, stretching)	40 (87%)
Cast immobilization	12 (26%)
Inlays	7 (15%)
Cortisone injection	13 (28%)
Rest	26 (57%)
NSAIDs	3 (7%)

Table 3. Number of injections per tendon

Number of injections per tendon	**Frequency (%)**
1	14 (26%)
2	11 (21%)
3	15 (28%)
4	6 (11%)
5	6 (11%)
6	0 (0%)
7	1 (1.9%)

Fifty-three symptomatic tendons were treated with a median of 3 sessions (range; 1-7) of Ethoxysclerol injections (Table 3). Fifty-six percent of patients rated the injections as unpleasant.

Short term results (6 weeks after the last injection)

All patients, except one, returned to work within 2 days after injection with Ethoxysclerol (median 0.0, range; 1-7 days). Of the 30 patients who were sports active before complaints, 18 patients (60%) resumed sporting activities, 12 (67%) at the same level, 5 (28%) on a lower level and 1 (5%) on a higher level. Median time to sports resumption was 2 weeks (0-104).

At 6 weeks follow-up 40 patients (45 tendons) showed up for US. Decrease of neovascularisation was present in 21 tendons (47%) (Table 4) and patients experienced pain relief in 19 treated tendons (44%): 15 (35%) caused no pain and 4 (9%) still produced minimal pain; 42% still experienced the same pain and 14% even had more pain.

Spearman's correlation coefficient showed a moderate correlation between the amount of neovessels observed on Doppler ultrasound and the pain level experienced by the patient ($r=0.48$, $p=0.001$).

Table 4. Information on the quantity of neovascularisation present 6 weeks after the last injection was present in 45 treated tendons. In 8 this outcome was not described

Neovascularisation 6 weeks after treatment	Tendons (n= 45)
No	5 (11%)
Less	16 (36%)
Same	20 (44%)
More	4 (9%)

Six weeks after treatment, significantly more male patients (58%) had no or minimal complaints than female patients (26%) (p=0.04). The odds ratio for females compared to males having the same or more complaints after treatment was 3.8 (95% CI 1.1-13.8), which means they had a 3.8 times higher chance of an unsatisfying outcome than males. Age did not significantly affect outcome (p=0.09). The median age of patients with no or minimal complaints after treatment was 43.5 (range; 33-68) years, and for patients with same or more complaints 49.0 (range; 35-60).

We could not identify a learning curve for performing the treatment. The outcome in the first 15 patients demonstrated that 56% to experienced no/minimal pain while 44% of patients demonstrated the same or more pain at follow-up. Results of treatment in the last 15 patients showed that 43% of these patients had none/ minimal pain whilst 57% had the same or more pain (p= 0.46).

Results at mid-term follow-up: 3.9 (range; 2.7-5.1) years

Median VISA-A score was 82 points (range; 20-100), median VAS for pain was 0 mm (range; 0-82) and for function 99 mm (range; 14-100).

Of the 40 tendons (of the 36 patients who had returned the questionnaire), 21 (53%) had additional treatment in the years following sclerosing injections. Fifteen tendons (71%) were treated operatively (open surgical debridement or Achilles tendoscopy), sometimes in combination with conservative treatment (2 tendons). The other 6 tendons (29%) were treated with different conservative measures. Of patients with 21 additionally treated tendons, 18 (86%) had the same or more complaints six weeks after injection and 3 (14%) had minimal complaints. Of patients with 19 tendons who did *not* report seeking additional treatment, 6 (32%) had same/more complaints and 13 (69%) had no complaints after six weeks follow-up. The 6 with same/ more complaints at six weeks had no complaints at mid-term follow-up without additional treatment.

The level of pain had significantly decreased at mid-term follow-up compared to six-week follow-up (p<0.01) (Diagram 1).

Of the 40 tendons at mid- term follow-up, 3 (7.5%) still showed the same or more complaints, even after additional surgical or conservative treatment.

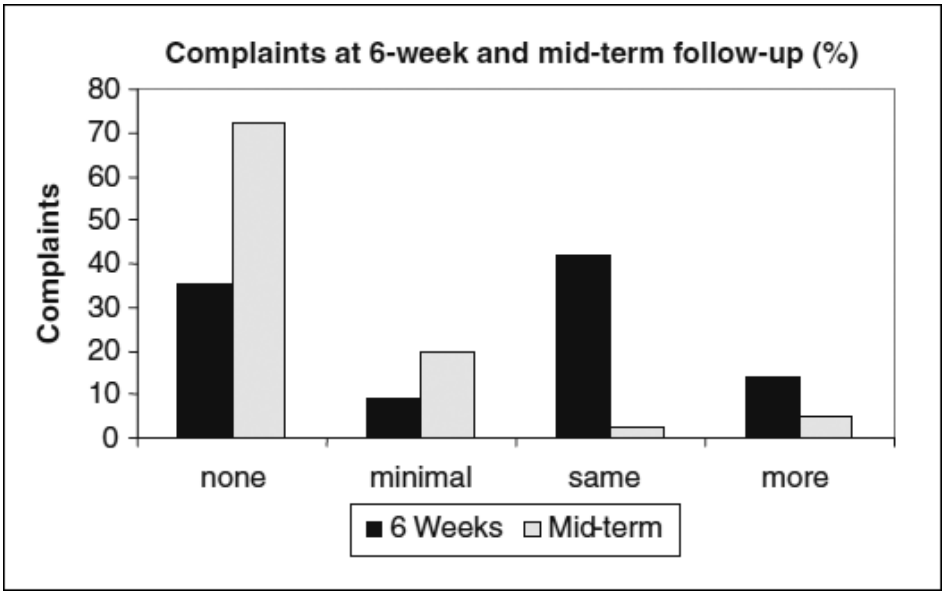

Diagram 1. Outcome of pain at 6 weeks and 2.7-5.1 years after sclerosing therapy

No significant correlations were observed between complaints at midterm follow-up and symptom duration, age, and BMI.

DISCUSSION

We could not demonstrate a beneficial effect of Ethoxysclerol injections in patients with mid-portion Achilles tendinopathy as opposed to earlier published results of this treatment[5,25]. Only 44% of tendons were painless or minimally painful at six weeks after treatment with Ethoxysclerol.

At 2.7-5.1 year follow-up 53% of *all* treated tendons had undergone additional treatment (nonoperative or surgical).

The treatment of chronic tendinopathy of the Achilles tendon with Ethoxysclerol as introduced by Alfredson and Ohberg in 2002 appeared to be a promising method of treatment[30]. It was hypothesized that neovessels and accompanying nerves were responsible for the pain in mid-portion Achilles tendinopathy. After a pilot study in 2002 in which they treated 10 patients, 8 of whom had favourable outcome, they further developed their technique resulting in a publication in 2005 in which the outcome of a double-blind randomised trial was published. Patients were injected with either Ethoxysclerol or lidocain combined with adrenalin[5]. The study showed that 10 out of 10 patients reported satisfaction with the result of the treatment with a significant improvement on VAS. Nine out of 10 patients in the control group reported

satisfaction, but the difference in VAS before and after the treatment in the Ethoxysclerol group was significantly larger. Also, patients in the sclerosing group showed no remaining neovascularisation on colour Doppler[5]. Extending their proposed pathophysiological principles of midportion Achilles tendinopathy and the role of neovessels in patellar tendinopathy they applied the same treatment regime of injecting a sclerosing agent into these patients in 2005, again with promising results[4]. In 2006, the group published the results of the first 2-year follow-up which showed remaining good clinical results and a lasting decrease in volume of the Achilles tendon. The favourable outcome in patients treated with this technique has also been published by Clementson and co-workers in 2008 in a retrospective study of 25 patients[9]. The technique has currently been introduced by Alfredson and co-workers for the treatment of painful tennis elbow and shoulder impingement syndromes[1,3,47]. All this suggests a beneficial value of Ethoxysclerol in midportion tendinopathy.

A possible reason for our less favourable outcome is the retrospective design of our study. We did not use neovascularisation scores or valid subjective outcome measures at six weeks follow-up. Treatment in our clinic was initially not set up as a clinical trail but we just implemented it as a new conservative measure for midportion Achilles tendinopathy. The reason for this was the high percentage of good and excellent results in various publications by the group of Alfredson indicating injection therapy to be a valuable treatment strategy. As opposed to a good outcome, patients reported low satisfaction all along the way. We considered this important to report, irrespective of the retrospective design.

Our success-rate from the injection of Ethoxysclerol is close to placebo-controlled studies on conservative measures such as corticosteroid injections and external triglyceryltrinitrate application, as well as the administration of placebo. These treatments also yield positive results in 33-49% of patients[10,32], well below the success percentage of eccentric training and various surgical approaches. Eccentric loading should be the very first treatment method for patients with midportion Achilles tendinopathy, since this treatment modality has been tested in a proper manner and yields good results[6,37-39]. However, the training programme is extensive, painful and requires strong perseverance. Eighty- seven percent of our patients reported to be subjected to an eccentric training program guided by a physiotherapist before being offered Ethoxysclerol injections, without a beneficial outcome. This may be a subgroup not responding to eccentric training, or it may be due to inadequate instructions or insufficient compliance.

Injection with Ethoxysclerol is a conservative treatment method and positive outcome in 44% of patients might be sufficient to implement this therapy as primary or secondary treatment option for some patients with symptomatic midportion Achilles tendinopathy. On the other hand, with an average of 2.7 injections with intervals of six to eight weeks it is an unpleasant

and time-consuming conservative treatment. This might particularly be problematic in active patients and professional athletes demanding a quicker solution to return to sports.

The origin of pain in midportion Achilles tendinopathy, its natural history and the mechanism by which a wide range of treatments generates relief is largely unknown. Sclerosing treatment is based on the hypothesis that neovessels at the ventral side of the Achilles tendon accompanied by nerves are the cause of pain. However, of 140 Achilles tendons with clinically and ultrasonographically demonstrated Achilles tendinopathy, only 70 tendons showed neovascularisation (50%). De Vos-, Peers-, Reiter- and Zanetti and co-workers found equal proportions of neovascularisation in 50-88% of symptomatic tendons[11,33,35,46].

The focus of treating Achilles tendinopathy is on relieving pain. Most often the intratendinous changes are addressed. However, it is questionable if degeneration of the tendon itself is the main cause of pain, since intratendinous changes are found in up to 34% of people *without* complaints[13,15,18,19]. Very recently a long-term follow-up study was published revealing persistent structural abnormalities and thickening of the tendon 13 years after intra-tendinous surgery for Achilles tendinopathy, whereas all patients were satisfied with the results and went back to Achilles tendon loading activities without restrictions[7]. Midportion Achilles tendinopathy and paratendinopathy often co-exist[43]. Adhesions between the tendon, peritendineum and crural fascia in the chronic phase are formed, prohibiting a normal gliding movement of the tendon. The healthy tendon proper is normally aneuronal[8], but chronic painful tendons have been shown to exhibit new ingrowth of sensory nerve fibers in the tendon proper[24,41]. We theorize that 'denervation' of the tendon is sufficient to relieve symptoms. With Ethoxysclerol, by addressing neovessels, nerves are probably also attacked. Injection may not suffice because of low volume and effectiveness of the substance on nerves, and adhesions are too solid to be adequately released.

In agreement with this theory, surgical release of these adhesions though an open approach[17,20,22,23,29,40] or via endoscopically assisted techniques[27,28,43,44], leaving the tendon proper untouched has demonstrated to be effective and provides quick rehabilitation. However, these series are small and follow-up is of short duration. Fundamental research and larger comparative series on surgical measures need to be done with proper study design and at least one year follow-up to verify the cause of complaints before optimal treatment can be developed.

CONCLUSION

Our study did not confirm a beneficial value of sclerosing Ethoxysclerol injections in patients with midportion Achilles tendinopathy. On the basis of our results, we decided to discontinue the implementation of this treatment in our clinic.

REFERENCE LIST

1. Alfredson H, Harstad H, Haugen S, Ohberg L. Sclerosing polidocanol injections to treat chronic painful shoulder impingement syndrome-results of a two-centre collaborative pilot study. Knee Surg Sports Traumatol Arthrosc 2006;14:1321-1326.
2. Alfredson H, Lorentzon R. Intratendinous glutamate levels and eccentric training in chronic Achilles tendinosis: a prospective study using microdialysis technique. Knee Surg Sports Traumatol Arthrosc 2003;11: 196-199.
3. Alfredson H, Lorentzon R. Sclerosing polidocanol injections of small vessels to treat the chronic painful tendon. Cardiovasc Hematol Agents Med Chem 2007;5:97-100.
4. Alfredson H, Ohberg L. Neovascularisation in chronic painful patellar tendinosis--promising results after sclerosing neovessels outside the tendon challenge the need for surgery. Knee Surg Sports Traumatol Arthrosc 2005;13:74-80.
5. Alfredson H, Ohberg L. Sclerosing injections to areas of neo-vascularisation reduce pain in chronic Achilles tendinopathy: a double-blind randomised controlled trial. Knee Surg Sports Traumatol Arthrosc 2005;13: 338-344.
6. 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;26:360-366.
7. Alfredson H, Zeisig E, Fahlstrom M. No normalisation of the tendon structure and thickness after intratendinous surgery for chronic painful midportion Achilles tendinosis. Br J Sports Med 2009;43(12):948-9.
8. Andersson G, Danielson P, Alfredson H, Forsgren S. Nerve-related characteristics of ventral paratendinous tissue in chronic Achilles tendinosis. Knee Surg Sports Traumatol Arthrosc 2007;15:1272-1279.
9. Clementson M, Loren I, Dahlberg L, Astrom M. Sclerosing injections in midportion Achilles tendinopathy: a retrospective study of 25 patients. Knee Surg Sports Traumatol Arthrosc 2008;16:887-890.
10. DaCruz DJ, Geeson M, Allen MJ, Phair I. Achilles paratendonitis: an evaluation of steroid injection. Br J Sports Med 1988;22: 64-65.
11. de Vos RJ, Weir A, Cobben LP, Tol JL. The value of power Doppler ultrasonography in Achilles tendinopathy: a prospective study. Am J Sports Med 2007;35:1696-1701.
12. de Vos RJ, Weir A, Visser RJ, de WT, 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;41:e5.
13. Emerson C, Morrissey D, Perry M, Jalan R. Ultrasonographically detected changes in Achilles tendons and self reported symptoms in elite gymnasts compared with controls - An observational study. Man Ther 2010;15(1):37-42.
14. Fahlstrom M, Jonsson P, Lorentzon R, Alfredson H. Chronic Achilles tendon pain treated with eccentric calf-muscle training. Knee Surg Sports Traumatol Arthrosc 2003; 11:327-333.
15. Haims AH, Schweitzer ME, Patel RS, Hecht P, Wapner KL. MR imaging of the Achilles tendon: overlap of findings in symptomatic and asymptomatic individuals. Skeletal Radiol 2000;29:640-645.
16. Hoksrud A, Ohberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. Am J Sports Med 2006;34:1738-1746.
17. Jarvinen M. Lower leg overuse injuries in athletes. Knee Surg Sports Traumatol Arthrosc 1993;1:126-130.
18. Kannus P, Jozsa L. Histopathological changes preceding spontaneous rupture of a tendon. A controlled study of 891 patients. J Bone Joint Surg Am 1991;73:1507-1525.

19. Khan KM, Forster BB, Robinson J et al. Are ultrasound and magnetic resonance imaging of value in assessment of Achilles tendon disorders? A two year prospective study. Br J Sports Med 2003;37:149-153.
20. Kvist M. Achilles tendon injuries in athletes. Sports Med 1994;18:173-201.
21. Langberg H, Bulow J, Kjaer M. Blood flow in the peritendinous space of the human Achilles tendon during exercise. Acta Physiol Scand 1998;163:149-153.
22. Leach RE, Schepsis AA, Takai H. Long-term results of surgical management of Achilles tendinitis in runners. Clin Orthop Relat Res 1992;282:208-212.
23. Lehto MU, Jarvinen M, Suominen P. Chronic Achilles peritendinitis and retrocalcanear bursitis. Long-term follow-up of surgically treated cases. Knee Surg Sports Traumatol Arthrosc 1994;2:182-185.
24. Lian O, Dahl J, Ackermann PW, Frihagen F, Engebretsen L, Bahr R. Pronociceptive and antinociceptive neuromediators in patellar tendinopathy. Am J Sports Med 2006;34: 1801-1808.
25. Lind B, Ohberg L, Alfredson H. Sclerosing polidocanol injections in mid-portion Achilles tendinosis: remaining good clinical results and decreased tendon thickness at 2-year follow-up. Knee Surg Sports Traumatol Arthrosc 2006;14:1327-1332.
26. 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; 9:42-47.
27. Maquirriain J, Ayerza M, Costa-Paz M, Muscolo DL. Endoscopic surgery in chronic achilles tendinopathies: A preliminary report. Arthroscopy 2002;18:298-303.
28. Morag G, Maman E, Arbel R. Endoscopic treatment of hindfoot pathology. Arthroscopy 2003;19:E13.
29. Nelen G, Martens M, Burssens A. Surgical treatment of chronic Achilles tendinitis. Am J Sports Med 1989;17:754-759.
30. Ohberg L, Alfredson H. Ultrasound guided sclerosis of neovessels in painful chronic Achilles tendinosis: pilot study of a new treatment. Br J Sports Med 2002;36:173-175.
31. 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;38:8-11.
32. Paoloni JA, Appleyard RC, Nelson J, Murrell GA. Topical glyceryl trinitrate treatment of chronic noninsertional achilles tendinopathy. A randomized, double-blind, placebo-controlled trial. J Bone Joint Surg Am 2004; 86-A:916-922.
33. Peers KH, Brys PP, Lysens RJ. Correlation between power Doppler ultrasonography and clinical severity in Achilles tendinopathy. Int Orthop 2003;27:180-183.
34. Perlick L, Schiffmann R, Kraft CN, Wallny T, Diedrich O. [Extracorporal shock wave treatment of the achilles tendinitis: Experimental and preliminary clinical results]. Z Orthop Ihre Grenzgeb 2002;140:275-280.
35. Reiter M, Ulreich N, Dirisamer A, Tscholakoff D, Bucek RA. [Extended field-of-view sonography in Achilles tendon disease: a comparison with MR imaging]. Rofo 2004; 176:704-708.
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;35:335-341.
37. 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;37:463-470.
38. 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: 374-383.
39. 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;14:286-295.
40. Schepsis AA, Leach RE. Surgical management of Achilles tendinitis. Am J Sports Med 1987;15:308-315.
41. Schubert TE, Weidler C, Lerch K, Hofstadter F, Straub RH. Achilles tendinosis is associated with sprouting of substance P positive nerve fibres. Ann Rheum Dis 2005;64:1083-1086.
42. Silbernagel KG, Thomee R, Thomee P, Karlsson J. 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;11:197-206.
43. Steenstra F, van Dijk CN. Achilles tendoscopy. Foot Ankle Clin 2006;11:429-38, viii.
44. van Dijk CN, Scholten PE, Kort N. Tendoscopy (tendon sheath endoscopy) for overuse tendon injuries. Oper Techn Sports Med 1997;5:170-178.
45. van LR, den Hoed PT, de Jongh AC. [Guideline 'Chronic Achilles tendinopathy, in particular tendinosis, in sportsmen/sportswomen']. Ned Tijdschr Geneeskd 2007;151: 2319-2324.
46. Zanetti M, Metzdorf A, Kundert HP et al. Achilles tendons: clinical relevance of neovascularization diagnosed with power Doppler US. Radiology 2003;227:556-560.
47. Zeisig E, Ohberg L, Alfredson H. Sclerosing polidocanol injections in chronic painful tennis elbow-promising results in a pilot study. Knee Surg Sports Traumatol Arthrosc 2006; 14:1218-1224.