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Research Article

Short- and Long-Term Effects of Sclerotherapy on Chronic Tendinosis with Neovascularization among Sportsmen and Athletes

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Abstract

When neovascularization is present in chronic tendinosis, sclerotherapy may be useful. This study's objective was to evaluate the short- and long-term clinical efficacy of sclerotherapy and estimate the evolution of Achilles and patellar tendinosis among athletes using ultrasound. All the patients who underwent sclerotherapy in our department from 2008 to 2017 were reevaluated.

Twelve patients met these inclusion criteria (15 tendons, 32 ± 21 years old, training 8.8 ± 12 h/week, symptom duration 38 ± 37.8 months). At week six, there was a significant mean reduction in exercise pain (visual analogue scale: from 7.7 ± 1.8 to 3.2 ± 2.3, $p = 0.0001$) with a resumption of sports by 12/15 patients, 6 at their previous level. At the long-term follow-up (45.5 ± 31 months), 12/15 had a clinically relevant decrease in exercise pain, with 6 partially resuming sports and 4 more resuming at their previous level (two with sclerotherapy alone). Vascularization scores objectivized by ultrasound decreased significantly from 3.38 ± 0.51 to 2.31 ± 1.23 ($p < 0.001$). Vessels only disappeared in 4/12 tendons, allowing 3 athletes to resume sports at their previous level. In conclusion, sclerotherapy appears to induce good short-term effects on pain and function. Long-term clinical effect is less obvious. Total disappearance of new vessels seems to be associated with a higher resumption of sports.

Keywords: Neovascularization; Sclerotherapy; Sport; Tendinosis; Ultrasound

Introduction

Tendinosis is a common work- and sports-related condition and a major cause of disability. More than 30% of sports-related injuries arise from or have an element of tendinopathy [1]. The pathogenesis of pain in tendinosis remains poorly understood, and it is probably multifactorial, associating intrinsic and extrinsic factors. This may explain the often-unsatisfactory results and the lack of a clear consensus on an evidence-based best treatment [2].

Lesions will often result in the appearance of neovascularization associated with neo-innervation, usually not found in normal, pain-free tendons whose blood flow might be altered during ankle dorsiflexion, such as that performed during eccentric exercise [3]

The persistence of these new vessels might be deleterious for tendon healing. Several publications have shown that symptoms can be improved by sclerosing these vessels with Aethoxysclerol® [2-8]. The disappearance of this neovascularization has been shown to favour the realignment of tendinous fibres and sometimes tendon repair or enthesis. Publications on this subject are nevertheless relatively scarce, show conflicting results and usually involve short-term follow-up only. Our department began to perform these alcohol infiltrations in 2008, mainly on athletes with chronic tendinopathies which remained resistant to any other usual treatments.

The present work aimed to evaluate the efficacy of alcohol sclerotherapy and estimate the short- and long-term evolution of the new vessels both clinically and using ultrasound.

Material and Methods

Design

This was a real-life observational study of all the patients who underwent sclerotherapy in our department from 2008 to 2017. Retrospective data on patients' pre-sclerotherapy presentation were extracted from their medical records. As a post-sclerotherapy follow-up, we used their medical files but also contacted the patients prospectively, offering them a check-up consultation involving a clinical evaluation and an ultrasound examination.

The study was approved by the Human Research Ethics Committee of the Canton Vaud (CER-VD: 2016 01432) and meets the ethical standards of the International Journal of Sports Medicine [9].

Patient Recruitment

Inclusion Criteria: All patients who had undergone one or more sclerotherapy treatments in our department, for chronic tendinitis and tendinopathy of the Achilles or patellar tendons, between 2008 and 2017, were eligible for inclusion, regardless of previous treatments and therapeutic approaches, whether medication, infiltration or physiotherapy.

Exclusion Criteria: Patients with a current inflammatory enthesopathy and those who refused to participate in the study after having given their consent were excluded.

Baseline Clinical Evaluation

At the initiation of sclerotherapy, the data recorded were age, sex, general health condition, possible comorbidities, sports practiced before the injury, estimated intensity of sporting activity in hours/week, and the ensuing degree of inability to practice that sport and disability in everyday life. Three degrees of disability were scored semi-quantitatively: 1 for a minor disability only present during intensive sports activity; 2 for moderate disability in recreational sports; and 3 for a major disability in all situations, including usual daily activities.

The average level of pain in the week preceding sclerotherapy was also evaluated according to the patient's personal feelings on a Visual Analogue Scale (VAS) from 0 to 10 (0 = not painful, to 10 = extremely painful). The duration between symptom onset and the first sclerotherapy, as well as between the last sclerotherapy and the follow-up visit, were calculated and expressed in months.

Ultrasound Examination

Tendons were examined using both B and Doppler modes. Each tendon was examined in the long- and short-axes by the same rheumatologist, highly experienced in ultrasound techniques. The examiner routinely measured tendon thickness and searched for areas of heterogeneous echogenicity, the possible presence of paratendinous fluid and calcification, and any other signs that may have indicated current or previous lesions

Using Doppler mode ultrasound, neovascularization (Figure1) was assessed using the semi-quantitative methodology previously defined and tested by Öhberg et al. in 2002 [3] and which classifies the appearance of vessels inside the tendons (0, 1+, 2+, 3+, 4+). The score was 0 when no vessels were visible; 1+ when one or two small vessels were present, mostly in the anterior part of the tendon; and 2+ to 4+ when there were several irregular vessels throughout the tendon. The ultrasound devices used were a Phillips HD1 and, from 2013 onwards, an Esaote MyLab 75.

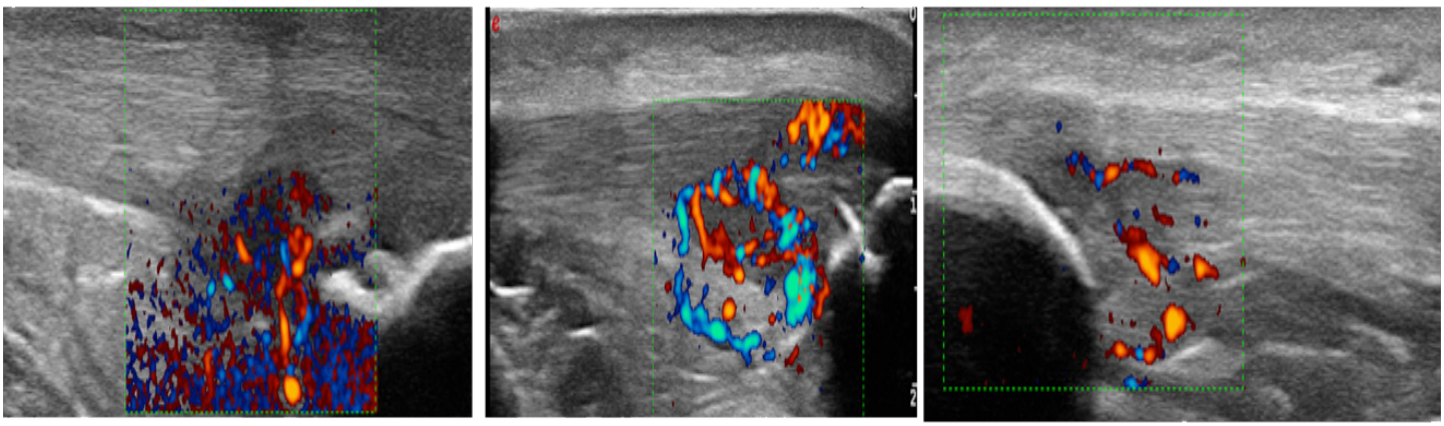

Figure 1: examples of neo vascularization that can be visualized by ultrasound, the vessels emerge from below the tendon and penetrate into it (Achilles: a; Patella: b and c).

Therapeutic Procedure

The sclerosing compound used was polidocanol (Aethoxysclerol® 0.5%,), with lauromacrogol 400 as the active substance at a concentration of 5 mg/ml. Skin was washed and disinfected before injection. Polidocanol was injected using a small volume needle, its length dependent on the depth of the new vessels relative to the skin. Local anesthesia was not used since polidocanol is anesthetic. The procedure was performed under ultrasound guidance and checking that pain disappeared immediately after the injection, thanks to the anesthetic effect of polidocanol.

The amount of liquid injected was not standardized but generally corresponded to that of commercially available bulbs (1-2 cc). Patients received 1-5 infiltrations with intervals of 15 days between each injection. After this, the case was re-evaluated, and other management options considered.

Short-Term Evaluation

After each injection, patients were recommended to remain relatively rested and, in particular, not to strain the treated tendon for two weeks. After this period, patients could resume their normal activities if the pain allowed them to. No restrictions were set as to the use of medication or anti-inflammatory creams.

The short-term evaluation was carried out an average of six weeks after the last sclerotherapy session. This included patients' self-assessments of perceived disability (as at the baseline visit) and of their ability to resume sports as before or their need to adapt those activities. Their recovery was classified into three categories: "no" if there was no resumption of sport; "partial" if recovery was partial or activities had to be adapted; and "yes" if the patient had been able to resume training and sports activities as before. Therapeutic approaches other than sclerotherapy, and their effects on symptoms, were also recorded. Finally, the residual pain level experienced by the patient was reassessed on the same VAS from 0-10 as a baseline.

Long-Term Follow-Up

The final follow-up visits occurred between October 2016 and October 2017. Clinical examinations and echographic evaluations were carried out by three rheumatologists who were also experienced musculoskeletal ultrasonographers. The ultrasound procedure performed was identical to that of the initial examination.

Statistics

Student's t-test or Fisher's exact test were used to compare qualitative variables, depending on the application. Qualitative and quantitative variables were compared using the Wilcoxon test or the Kruskal-Wallis test, depending on the number of classes of qualitative variables (> or < 2). Statistical analysis was performed using SAS software, v9 (SAS Inst., Cary, NC, USA) for Windows XP. The significance threshold was set at $p < 0.05$.

Results

Baseline Clinical and Demographic Data

Of the 14 patients who had received sclerotherapy, 12 accepted to participate in the study (two women, ten men). As three patients had bilateral chronic tendinopathies, a total of 15 treated tendons were evaluated: 11 patellar tendons and 4 Achilles tendons They were mainly young, with heavy training schedules before the onset of tendinopathy (8.8 ± 12 h/week), 4 being elite athletes and 2 being sports teachers. Median age was 32 years old. The sports practiced were basketball (5/15), running (3/15) and soccer (3/15), and some patients practiced several sports. Mean symptom duration was 32 months (range 6-168) before sclerotherapy was started. The median number of sclerotherapy sessions performed was three.

At baseline, before the first sclerotherapy treatment, pain was described as high (≥ 7/10 on the VAS for pain) during exercise for 13/15 tendons (mean 7.7 ± 1.8), but very low at rest (mean 1.7 ± 2.09). The disability score was moderate (or 2) in 73% of tendons, leading to a decrease in sports activities.

Before trying sclerotherapy, in 9/15 cases, patients had used non-steroidal anti-inflammatory drugs in topical, patch or tablet form; 13/15 had had physiotherapy; 6/15 had extracorporeal shockwave therapy; and 6/15 had already received corticosteroid injections. Patients reported that most of the time these treatments helped to temporarily relieve pain, but that tendinopathy started again as soon as they resumed their usual training schedule. In a third of cases, tendinopathy was very resistant to these treatments. Finally, 2 patients (2 tendons) underwent no other treatments before sclerotherapy.

Clinically, each patient had tendinopathy involving a thickened tendon and pain on palpation.

Short-Term Follow-Up

All patients underwent a short-term follow-up at 6 weeks. The number of infiltrations carried out varied from 1-5 (mean 3). No patients reported any side effects related to the injection and, importantly, no tendon rupture. The pain described during sports activities clearly improved in 12/15 tendons. The mean VAS pain scores were 3.22 ± 2.31 during exercise and 0.26 ± 0.58 at rest. The change was significant, both for rest pain ($p = 0.01$) and exercise pain ($p = 0.000002$).

Patients experienced a positive clinical improvement in 40% (6/15) of the tendinopathies studied, with an almost complete disappearance of pain. A partial improvement in symptoms

was reported in 33% of tendinopathies, and 27% reported no improvements in their pain (VAS change < 2/10). The resumption of sport after sclerotherapy sessions was possible in 12/15 cases, 6 at their previous level and 5 less intensely. In 3/15 cases, however, a resumption of sport remained impossible. One patient had to change the sport which he had previously practiced.

Long-Term Follow-Up

The mean duration of follow-up after the first sclerotherapy session was 43.7 ± 31 months. An improvement in pain symptoms was reported in 12/15 initial tendinopathies (VAS change > 3/10). The improvement was sufficient to allow a resumption of the same sport in 10 cases. However, recovery was complete and without any residual pain in only 4 cases. Also, only 2 of them were fully relieved by sclerotherapy, without additional treatment. Only for 5/15 tendinopathies no other means of treatment after sclerotherapy were used. The others required one or more treatments, as follows: 8 physiotherapies, 2 platelet-rich plasma injections, 2 extracorporeal shockwave therapies, 1 corticosteroid injections, 1 mesotherapy, 1 osteopathy, and 1 a surgical intervention (Table 1).

Tendons	Neovascularization Initial (Grade0-4)	Neovascularization Final (Grade0-4)	Additional Treatment	Sport Recovery
1	3	2	Physiotherapy prp	total
2	3	0	Physiotherapy surgery	total
3	3	1		stop
4	4	3		stop
5	4	2		stop
6	3	0		total
7	3	0		total
8	4	0	physiotherapy mesotherapy	stop
9	3	2	prp	total
10	4	1	Physiotherapy shockwave	partial
11	4	3	Physiotherapy Steroid infiltration	partial
12	3	3	physiotherapy	partial
13	3	1	Physiotherapy shockwave	partial
Total (mean /SD)	**3.38 /0.51**	**1.31/1.23**		

Table 1: Echograhic evolution of neovascularization, additional treatments reported and recovery of sport at the final visit.

The mean follow-up time for the 4 patients who were able to resume their sports activities totally was not different from that of the rest of the group (52 ± 33 months). The time from symptom onset to sclerotherapy ranged from 6 to 168 months the mean symptom duration for the 4 patients who were able to resume their sports activities fully was 9.83 months (SD 2.71; median, 11), whereas the mean of the 4 people who had to stop sport totally was 43.5 months (SD 44.65; median 39).

Baseline and Final Echographic Evaluations

Using ultrasound in B-mode at baseline, the tendons were abnormal in all the patients. The images revealed either a distal or proximal focal hypoechoic appearance, sometimes with a loss of fibrillary structure and signs of calcification. Using color Doppler ultrasound showed neovascularization in all of them. The mean initial neovascularization score ± standard deviation, according to the Öhberg classification, was 3.38 ± 0.51.

During the final visit, two patients refused to undergo a new ultrasound examination. Eight of the 13 reevaluated tendons remained thickened (as were all the tendons at the time of sclerotherapy). Seven of the 13 tendons had a focal hypoechoic appearance, 1 had a rather hyperechoic appearance, and only 1 tendon had a normal appearance without evidence of injury.

The mean final neovascularization score (2.31 ± 1.23) was significantly lower than the baseline score (0.38 ± 0.51) ($p < 0.001$). Neovascularization had completely disappeared in 4/13 cases and decreased in 9/13 treated tendinopathies. Three of the 4 patients who were able to resume their sports at their previous levels had no residual neovascularization; 2 of them had been treated using

sclerotherapy alone. The 6 cases with partial sports recovery had persistence of some neo-vessels. (see details in Table)

Discussion

In this small cohort of athletes, sclerotherapy to treat neovascularization in Achilles and patellar tendinosis led to mixed results. We evidenced a significant and clinically relevant decrease in exercise-related tendon pain at 6-weeks follow-up, with 80% of patients (12/15) resuming their sports activities, half of them at the previous level. However, this positive effect did not seem to be maintained over time, as many patients had to use other therapies, and only 2 patients were completely relieved of pain and able to resume their previous level of sports activity following sclerotherapy alone. These results seem to be inferior to those previously reported in other studies of patellar tendinosis [4,5,10] or Achilles tendinosis [2-4,6-8], which reported positive effects in up to two thirds of cases [4].

This apparent discrepancy is probably explained by distinct study designs (real-life versus prospective study) [11], sample differences (our study's athletes had very long symptom duration before sclerotherapy), and our patients' very long follow-up (mean > 40 months). Mean duration of follow-up was only 3 months in Öhberg's initial randomized study [3] and 6 months in Hoksrud et al.'s [11] initial study. Nevertheless, in a subsequent study with a 24-month follow-up, the same author noted little healing and the persistence of pain in most patients, as observed in our series [4]. As mentioned in the results, the long time between symptom onset and sclerotherapy endured by most of our patients probably played a major role in their unsatisfactory long-term response to therapy. This delay seemed to be an important influence on outcomes. Good long-term clinical responses were mainly obtained when the procedure was applied within one year of symptom onset.

Moreover, given our real-life study and the duration of follow-up, it was impossible to control or standardize adjuvant treatments. Indeed, more than 50% of patients used pre- and/or post-sclerotherapy treatments, and 30% had to reduce their training schedule or adapt their physical activity to reduce their level of pain. The relationship between neovascularization and symptoms is not very clear in the literature [12]. In the present study, only 4/12 patients had no residual vascularization at their follow-up visit. Hoksrud, et al. [13] found a similar proportion, with 35% of sclerotherapy-treated tendons showing no residual tendon vascularization. Although it was difficult to correlate the ultrasound examination images with patients' clinical evolution, due to the small, heterogeneous sample of patients, it is noteworthy that three quarters of the patients who were able to resume their sports activities completely had no residual vascularization.

Our study has several major limitations, including relatively few patients and a lack of standardized adjuvant therapies. The chronologies and contexts of each tendinopathy were also different for each participant. Although we were unable to have a control group, our results reflected the difficulties of managing this type of pathology in real life and its applicability in this context outside of randomized studies. With regards to the use of ultrasound, the main limitation was that the sensitivity of the different Doppler devices used during the study had increased significantly over time. This could have led to an overestimation of residual Doppler echogenicity in comparison to the initial evaluation.

Conclusion

In conclusion, the results of the present real-life study were consistent with those of previous studies. Sclerotherapy is a treatment with no side effects and with a good short-term impact on pain and function in patients suffering from chronic tendinopathy with neovascularization. The long-term effects on clinical symptoms and neovascularization, however, are less obvious. A longer duration between symptom onset and sclerotherapy seems to have a negative influence on long-term results. Neovascularization may persist despite sclerotherapy. The disappearance of new vessels could be a criterion for a positive clinical evolution. Controlled studies to better specify the predictive criteria for good clinical response by all tendinopathies are to be recommended.

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