High-volume injection in the management of recalcitrant mid-body Achilles tendinopathy: a prospective case series assessing the influence of neovascularity and outcome

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Objectives: To determine the effectiveness of ultrasound-guided high-volume injection (HVI) and relevance of neovascularity on outcome in Achilles tendinopathy.

Methods: This prospective clinical study at the Homerton University Hospital included 32 patients with recalcitrant unilateral mid-substance Achilles tendinopathy. Outcome measures used were Victorian Institute of Sport Assessment-Achilles tendon (VISA-A), Visual Analogue Score (VAS), modified Öhberg score and mean maximum tendon thickness.

Results: Significant improvements in both VAS and VISA-A scores at 1 month (95% confidence interval (CI), 6.6–3.2, \( P < 0.001 \) and 37.2–63.7, \( P < 0.001 \)). This improvement was maintained at 3 months (95% CI, 6.6–2.9, \( P < 0.001 \) and 37.2–65.9, \( P < 0.001 \)). Symptomatic tendons were significantly thicker at baseline than the asymptomatic side (95% CI, 8.3 mm compared to 5.9 mm, \( P < 0.001 \)). There was a significant decrease in maximum tendon thickness in the symptomatic tendons at baseline and at 3 months (95% CI, 8.3–7.6 mm, \( P < 0.001 \)). Mean Öhberg neovascularity scores demonstrated a significant decrease between baseline and 3 month review (95% CI, 2.5–1.1, \( P < 0.001 \)). There was a significant difference in neovascularity at baseline for the symptomatic and asymptomatic sides (95% CI, 2.5 compared to 0.2, \( P < 0.001 \)). There was a positive correlation between baseline neovascularity and difference in VAS scores at baseline and 3 months. Patients with higher baseline Öhberg scores demonstrated a more positive outcome (95% CI, correlation coefficient 0.696, \( P < 0.01 \)).

Discussion: Ultrasound-guided HVI is safe and clinically cost-effective in treating Achilles tendinopathy. Results suggest that baseline neovascularity is relevant to outcome following injection.

Keywords: Achilles tendinopathy, Chronic, High-volume injection, Neovascularity, Treatment

Introduction

Chronic Achilles tendon pain is a common disorder among both recreational and professional athletes with an estimated 18% of all lower-limb injuries in recreational runners involving the Achilles tendon.\(^1\,^2\) Although the prevalence of Achilles tendon pain appears to be higher in recreational and professional athletes than in those individuals who participate in little or no regular exercise, studies have demonstrated that up to 33% of patients who complain of Achilles tendon pain do not partake of any regular physical activity.\(^3\,^6\) Achilles tendon pain appears to occur in both male and female populations of all ages, but seems to be a particular problem in men aged between 35 and 45 years.\(^7\,^8\)

Although the pathological changes associated with tendinopathy are poorly understood, it is generally accepted that in the chronically injured tendon the repair capacity of the tendon is exceeded. Histological examination of tendon tissue in symptomatic individuals consistently shows either absent or minimal inflammation.\(^9\,^12\) Rather Achilles tendon pain seems degenerative in nature. These pathological changes are not limited to the Achilles tendon,\(^10\,^11\) but have also been identified in the rotator cuff of the shoulder,\(^12\) patellar tendon of the knee\(^13\) and the common extensor tendon of the elbow.\(^14\) When seen in the Achilles tendon the degenerative change has been described as being a combination of both
intratendinous lesions and thickening and adhesion around the paratenon. This is demonstrated particularly between the paratenon and the crural fascia. Intratendinous degeneration consists of tenocyte hyperplasia with prominent neovascularization, and endothelial hyperplasia. In light of the lack of inflammatory cells found, the term tendinitis would seem to be inappropriate and misleading. Rather the term tendinopathy would seem the more accurate descriptor and is increasingly being used to describe Achilles tendon pain.

In terms of clinical relevance the degree of tendon thickening and associated intratendinous degenerative change have been shown to impact negatively on outcome. However, increased neovascularity, as established in both patella and Achilles tendons, seems to be of less clear clinical relevance with Zanetti demonstrating that although neovascularity appeared to be a specific sign for tendon pain it did not indicate an unfavourable outcome in the Achilles tendon following conservative treatment consisting of exercise and physiotherapy.

There is no single, specific test for Achilles tendinopathy with clinical assessment remaining the mainstay of diagnosis. Ultrasonography (US) has increasingly been used to grade pathological changes with regard to tendon thickening with changes in tendon echogenicity indicating the presence of tendinosis, partial and complete tearing. In addition to grey-scale changes, Power Doppler assessment provides a means to measure the degree of neovascularity within and around tendons.

However, the relevance of this neovascularity in tendinopathy remains unclear as does subsequent change in the degree of neovascularity present in tendons following intervention. Öhberg reported neovascularity to be present in all symptomatic Achilles tendons that subsequently decreased with a concurrent reduction in symptoms following conservative treatment. Alfredson noted that the degree of neovascularization of Achilles tendons increased within the first 3 weeks following sclerosing injections although this subsequently decreased at further review. These findings would suggest some possible short-term benefit of neovascularity in the early stages following treatment. A number of measurement scales have been suggested as tools by which the degree of neovascularization present may be recorded. Although all these measures include a degree of subjectivity, one, the modified Öhberg score of a simple 5-point scale, has been shown to have excellent interobserver reliability.

The management of Achilles tendinopathy mostly relies on conservative therapeutic interventions, including therapeutic ultrasound, deep transverse friction massage, flexibility exercises, orthotics, and eccentric loading of the tendon. At present, eccentric overload exercise is widely used in clinical practice: however, the exact mechanism of how eccentric loading of the Achilles tendon results in a direct histological effect with concurrent decrease in pain and increase in reported function remains unclear. Although the general consensus has until recently been that eccentric exercises are able to generate greater forces within the tendon than concentric exercises, a recent study by Rees demonstrated that this was not the case and that peak tendon forces in eccentric exercise were of the same magnitude as seen in concentric exercise. Intriguingly Rees did note a pattern of sinusoidal loading and unloading in eccentric exercise that was not demonstrated in concentric exercise and proposed that these fluctuations in force may provide the stimulus for tendon regeneration. In a systematic review of the literature Kingma examined nine clinical trials but found that only one was considered to be of a high methodological rigour. Although this trial did demonstrate a positive outcome in favour of eccentric loading, the conclusion of the authors was that larger trials, with better methodology, were required.

Surgery is considered when conservative therapies fail with techniques including debridement of pathological peritendinous tissue, decompression of central tendon lesions and tendon augmentation with fascial strips of the gastrocnemius soleus complex. Excision of the pathological peritendinous tissue and longitudinal incisions of the tendon in isolation or with excision of the intratendinous lesion are perhaps the surgical procedures most commonly performed. Alternative procedures include excision of intratendinous lesions either with augmentation using tendon or fascia or without augmentation. Multiple longitudinal incisions of the tendon have also been performed percutaneously.

The aim of this prospective clinical study was to evaluate the efficacy of an ultrasound-guided high-volume injection (HVI) in the treatment of recalcitrant mid-substance Achilles tendinopathy and to evaluate the clinical relevance of the degree of neovascularity present at baseline with perceived outcome following treatment.

**Methods**

**Patients**

Patients were included in the study if they had been given a diagnosis of mid-substance Achilles tendinopathy from those attending the Homerton University Hospital Sports and Musculoskeletal Clinic between September 2010 and February 2011. This clinical diagnosis had to be confirmed on ultrasound examination. All agreed to participate in the prospective follow-up after full explanation of the study. Patients were excluded if they had a previous injection or surgery or if they had bilateral symptoms.
All patients must have been prescribed a course of eccentric exercise and continued with this programme for at least 3 months prior to inclusion, but at this point had either failed to continue due to lack of perceived improvement or pain.

**Ethics**

Consultation with the Local Ethics Committee determined that ethical approval was not required as the study involved no additional treatment and no treatment was withheld from patients. Patient notes were held in accordance with current NHS guidelines. Results generated from the study were stored in strict confidentiality and coded in such a way that patients could not be identified from the final collated data.

**Intervention**

Following explanation of the procedure HVI was then performed. Under ultrasound guidance the site of maximal tendon thickness was identified and using a medial approach the anterior edge of the tendon was injected (Figs. 1 and 2). In total injection consisted of 25 mg of hydrocortisone, 5 ml of 1% lignocaine and up to 40 ml of normal saline.

Needle placement was directed by a first operator under ultrasound guidance and the injection given by a second operator using low-pressure tubing (Angiotech, connecting tube, Mana-Tech Ltd.). This enabled the necessary pressure to be applied to the syringe during injection without unnecessary needle movement (Figs. 3 and 4).

Post injection patients were advised to refrain from exercise for 3 days but allowed to partake in normal activities of daily living. For a further 3 days they were advised to return to their eccentric programme of exercise only. Then 3 days of eccentric exercise and low-impact exercise were followed by a slow return to normal exercise as pain allowed. The eccentric exercise programme was to be continued for 3 months.

The eccentric programme prescribed consisted of four sets of 20 repetitions of Achilles loading with the knee straight and a further four sets of 20 repetitions with the knee bent. These exercises were to be carried out at a level that was uncomfortable and for one session per day.

**Study protocol**

Each patient was examined pre-injection and at 1- and 3-month follow-up. The study protocol was the same...
at pre-injection and at 1- and 3-month follow-up. It consisted of the following assessments and outcome measures being utilized.

**VAS and VISA-A**
The visual analogue scale (VAS) consisted of a line exactly 100 mm long. The patient was asked to place a mark on the scale that represented the severity of their pain at that time. The scale ran from no pain to severe pain. The VAS is generally believed to work adequately for acute pain states. The Victorian Institute of Sport Assessment-Achilles (VISA-A) questionnaire was developed specifically for evaluation of Achilles tendon pathology and consists of eight questions includes elements that assess pain and function. It has been demonstrated to be a valid and reliable index of the clinical severity of Achilles tendinopathy.

**Achilles tendon diameter**
Measurement of the maximum anterior to posterior tendon thickness took place in the transverse plane (Fig. 5).

**Ultrasound and neovascularity**
All US examinations were performed by one of the authors, an experienced musculoskeletal sonographer with several years experience using a Siemens Acuson X300 with a VF13-5 linear probe. US examinations were performed bilaterally at initial assessment prior to injection and repeated at 1- and 3-month review. Patients were asked to lay prone on the examination couch with their feet freely hanging over the edge of the couch in a neutral position. The initial US assessment utilized Power Doppler imaging to assess for neovascularity. This was carried out prior to assessment for tendon homogeneity and tendon thickness to avoid occlusion of the neovessels that may have occurred if the foot was dorsiflexed. No pressure was applied to the foot while assessment of neovascularity took place. The Doppler gain was set just below background noise at 3 dB. Following assessment for neovascularity the foot was positioned at 90° and the tendon was assessed for homogeneity and thickness.

The degree of observed neovascularity with Power Doppler was measured using the 5-point modified Öhberg score. This scoring system is outlined in Table 1.

An example of a modified Öhberg score 4+ is demonstrated below (Figs. 6 and 7).

### Table 1 The modified Öhberg score for tendon neovascularity

<table>
<thead>
<tr>
<th>Score</th>
<th>Descriptor</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>No vessels visible</td>
</tr>
<tr>
<td>1+</td>
<td>One vessel visible mostly anterior to the tendon</td>
</tr>
<tr>
<td>2+</td>
<td>One or two vessels throughout the tendon</td>
</tr>
<tr>
<td>3+</td>
<td>Three vessels throughout the tendon</td>
</tr>
<tr>
<td>4+</td>
<td>More than three vessels throughout the tendon</td>
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</tbody>
</table>

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**Figure 4** Left Achilles tendon immediately post-injection demonstrating significant swelling. (Source: Photograph taken in Sports and Musculoskeletal Medicine Department at the Homerton University Hospital).

**Figure 5** Transverse image of Achilles tendon demonstrating a significant anterior-to-posterior thickening. The two crosses represent the measurement callipers and record a distance of 8.2 mm. (Source: Image from Sports and Musculoskeletal Medicine Department at the Homerton University Hospital).

**Figure 6** Longitudinal image of an Achilles tendon demonstrating a florid neovascularity with significant thickening. The modified Öhberg score for this tendon was 4+. (Source: Image from Sports and Musculoskeletal Medicine Department at the Homerton University Hospital).
Statistical analysis was performed using SPSS version 16 (SPSS Science, Chicago, USA) and significance was assumed for all measures when $P$ values were less than 0.05. An initial Kolmogorov–Smirnov test was carried out to assess for the degree of normality of the distribution of the data.

The difference between baseline, 1- and 3-month review VAS and VISA-A scores was analysed. For statistical purposes, these data were considered to be non-parametric in nature and were analysed using the Wilcoxon Signed Ranks Test. Baseline and 3-month review Öhberg scores for symptomatic and asymptomatic tendons were also considered non-parametric in nature and were analysed using the Wilcoxon Signed Ranks Test. Tendon diameter at baseline and 3-month review for both symptomatic and asymptomatic patients was considered parametric and analysed using the paired sample $t$-test.

The difference between the baseline and 3-month review VAS scores was calculated for each patient and examined for correlation with that subject’s baseline Öhberg score to explore whether the degree of neovascularity at baseline influenced outcome. For the purposes of statistical analysis, the data were treated as non-parametric and were analysed using Spearman’s rho test.

Figure 7 Transverse ultrasound image of a symptomatic Achilles tendon. Power Doppler imaging demonstrates neovascularity originating from the anterior region of the tendon. Note also the posterior enhancement suggesting poor-quality tendon tissue at this level. (Source: Image from Sports and Musculoskeletal Medicine Department at the Homerton University Hospital).

Figure 8 Patient progress through the study.

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Results

Patients
The flow diagram (Fig. 8) demonstrates the progress of patients through the study with details of those who were not included in the final analysis of results. During the study, no patients were lost to final follow-up. Two patients who described a poor outcome to treatment opted for referral for a surgical opinion. Baseline patient demographics are shown in Table 2.

Mean VAS and VISA-A scores pre-injection, 1- and 3-month review
Mean VAS scores decreased significantly from baseline to 1-month review (95% confidence interval (CI), 6.6–3.2, \( P < 0.001 \)) a trend that was maintained at 3-month review (95% CI, 6.6–2.9, \( P < 0.001 \)) (Graph 1).

Concurrently the mean VISA-A scores increased significantly from baseline to 1-month review (95% CI, 37.2–63.7, \( P < 0.001 \)) a trend that was maintained at 3-month review (95% CI, 37.2–65.9, \( P < 0.001 \)) (Graph 2).

Mean maximum tendon diameter
There was a significant decrease in the mean maximum tendon diameter from baseline to 3-month review (95% CI, 8.3–7.6 mm, \( P < 0.001 \)). Likewise, a significant difference was also seen between the mean maximum tendon thickness at baseline for the symptomatic and asymptomatic sides (95% CI, 8.3 mm compared to 5.9 mm, \( P < 0.001 \)) (Graph 3).

Mean Öhberg neovascularity scores
There was a significant decrease in the mean Öhberg neovascularity scores between baseline and 3-month review (95% CI, 2.5–1.1, \( P < 0.001 \)). There was also a significant difference between the mean scores at baseline for the symptomatic and asymptomatic sides (95% CI, 2.5 compared to 0.2, \( P < 0.001 \)) (Graph 4).

The relationship of tendon neovascularity at baseline and outcome
There was a significant correlation between the baseline Öhberg neovascularity scores and difference in baseline and 3-month review VAS scores, such that patients with higher baseline Öhberg scores demonstrated a trend to a more positive outcome (95% CI, correlation coefficient 0.696, \( P < 0.01 \)) (Graph 5).

There was no correlation between the Öhberg neovascularity scores at baseline and duration of reported symptoms (correlation coefficient –0.074, \( P < 0.686 \)) or the self-reported baseline VAS and VISA scores.

Table 2 Patient characteristics and outcome variables at baseline (pre-HVI)

<table>
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<th>Variable</th>
<th>Value</th>
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<tr>
<td>Mean age (years) (range)</td>
<td>40.3 (25–63)</td>
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<tr>
<td>Gender</td>
<td>20 male/12 female</td>
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<tr>
<td>Mean duration of symptoms (months) (range)</td>
<td>17 (6–60)</td>
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<tr>
<td>Active in sports (%)</td>
<td>20 (62.5)</td>
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<tr>
<td>Mean tendon thickness symptomatic side (mm) (range)</td>
<td>8.4 (5.7–10.5)</td>
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<tr>
<td>Mean tendon thickness asymptomatic side (mm) (range)</td>
<td>5.7 (4.7–7)</td>
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<td>Mean Öhberg score symptomatic side</td>
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<tr>
<td>Mean Öhberg score asymptomatic side</td>
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<tr>
<td>Mean VAS score (range)</td>
<td>6.6 (4–9)</td>
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<tr>
<td>Mean VISA-A score (range)</td>
<td>37.2 (10–60)</td>
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</tbody>
</table>

Graph 1 Mean VAS scores at baseline, 1 and 3 months review.

Graph 2 Mean VISA-A scores at baseline, 1 and 3 months review.

Graph 3 Mean Achilles diameter (mm) of the asymptomatic and baseline and 3-month review symptomatic Achilles tendon.

Graph 4 Mean Öhberg score of the asymptomatic and baseline and 3-month review symptomatic sides.
changes in perceived outcome. In an attempt to the effects of the HVI resulting in the subsequent eccentric exercise programme and the inclusion of activity. Patients were asked to continue with their true control group matched for age, sex, and physical activity. Secondly, this study is limited by the absence of a long-term follow-up (mean 30.3 weeks). Similarly, our study noted no significant post-HVI complication other than some immediate post-injection soreness. Paavola documented an overall complication rate of 19% with delayed wound healing being the most common problem. This complication appeared to be more prevalent in patients who had a combination of both peritendinous adhesions and intratendinous lesions (27%) than in those patients with peritendinous adhesions only (6%).

In addition to the increased possibility of complication, surgery is also more expensive than HVI and results in a longer period of rehabilitation prior to the patient being able to return to sport. In our study, patients recommenced their eccentric exercises immediately following the HVI and were advised to return to low-impact exercise within 3 days, gradually increasing this as pain allowed.

Besides surgical intervention, other treatment interventions for recalcitrant Achilles tendinopathy that have been proposed include injection of platelet-rich plasma (PRP). This is defined as a concentrated injection of platelets, which have the ability to release several growth factors that in theory enhances the tissue repair processes and subsequent tendon integrity. Although in vitro evidence suggests that PRP may lead to an accelerated remodelling of damaged tendon with concurrent vascularization, this has not been demonstrated in the clinical setting. Indeed, de Vos concluded that PRP does not contribute to increased tendon structure or alter the degree of neovascularization present when compared with placebo.

The clinical relevance of this increased neovascularization in tendons is uncertain. Movin found an increase in the neovascularity present in 26 of the 40 tendon samples obtained during semi-quantitative histological analysis of symptomatic Achilles tendons. This finding was supported by Zanetti, who found...
that neovascularisation was present in 33 of 55 painful Achilles tendons but in only 1 of 25 asymptomatic tendons. Although this strongly suggests that neovascularity is a good indicator of pain the authors found no indication that this increase in tendon vascularization was associated with poor outcome. Indeed, our study would suggest that the greater the initial degree of neovascularization present the more positive an outcome may be expected. Although this finding may be specifically related to the use of HVI it could also reflect the fact that those patients with a higher initial tendon neovascularity have a greater degree of pathological change present and if this is associated with greater symptoms may also be a reflection of these patients having more to gain following HVI.

The location of the neovessels appears more marked within the anterior region of the tendon.20,21 This observation is supported by the findings of our own study. Although we did not specifically assess tendons for the location of neovascularity, Doppler imaging confirmed that this was predominantly located within the anterior region (Figs. 6 and 7).

The prevalence of anteriorly located neovascularity has implications with regard to treatment and in terms of pathological process. The HVI outlined in our study is given at the anterior edge of the Achilles tendon at its interface with the anterior peritendinous tissue and Kager’s fat. Immediately post–HVI and the neo-vessels are seen to have disappeared on Doppler imaging. It could be argued that the pressure of the injected fluid is sufficient to temporally compress and therefore occlude these neovessels. Indeed, firm pressure with the ultrasound transducer is often sufficient to reproduce this effect without injection. However, the decrease in neovascularity in our study was still significantly reduced at 3 months ($P < 0.001$) long after the injected fluid had been absorbed.

Theoretically then HVI may result in the neovessels being stripped from the anterior aspect of the tendon and that this leads to an alteration in the failing tendon repair process with subsequent regeneration of more normal, healthy tissue. Conversely, as the neo-vascular vessels are stripped from the anterior tendon then there is also a stripping of the associated neo-neural tissue. This would result in denervation of the painful tendon that may also have a positive effect on tendon regeneration but would also allow patients to perform a programme of eccentric loading more effectively and with greater compliance. The relatively rapid improvement in symptoms post-injection noted in our study and that of Chan20 would suggest that although HVI may have a primary and direct effect on tendon pathogenesis, denervation of painful tendon tissue maybe the primary treatment effect. The changes noted subsequently, such as a decrease in tendon diameter and decrease in the neovascularity represent secondary change.

In conclusion, this prospective follow-up study demonstrated that US-guided HVI appears to be a safe and clinically cost-effective treatment option in the management of recalcitrant mid-substance Achilles tendinopathy when delivered in conjunction with an eccentric exercise programme. In addition, our study suggests that the degree of neovascularity as measured by the modified Öhberg score appears to be related with regard to outcome such that greater initial neovascularity predisposes a more positive outcome. This finding may help clinicians and patients in deciding whether or not to proceed with injection when discussing possible treatment options.

Given the limitations of our study randomized trials with a non-injected control group, matched for age, sex and physical activity with longer-term follow-up are required to further determine the value of HVI in the treatment of recalcitrant Achilles tendinopathy.

References


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