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HOT TOPIC

Dry Needling as a Treatment Modality for Tendinopathy: a Narrative Review

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Abstract

Purpose of Review Tendinopathy describes a combination of pain, swelling, and impaired performance of the tendon and around structures. There are various treatment options for tendinopathy with unclear efficacy. Dry needling involves inserting needles into the affected tendon, and it is thought to disrupt the chronic degenerative process and encourage localized bleeding and fibroblastic proliferation. The purpose of this review is to review the use of dry needling as a treatment modality for tendinopathy.

Recent Findings The effectiveness of dry needling for treatment of tendinopathy has been evaluated in 3 systematic reviews, 7 randomized controlled trials, and 6 cohort studies. The following sites were studied: wrist common extensor origin, patellar tendon, rotator cuff, and tendons around the greater trochanter. There is considerable heterogeneity of the needling techniques, and the studies were inconsistent about the therapy used after the procedure. Most systematic reviews and randomized controlled trials support the effectiveness of tendon needling. There was a statistically significant improvement in the patient-reported symptoms in most studies. Some studies reported an objective improvement assessed by ultrasound. Two studies reported complications.

Summary Current research provides initial support for the efficacy of dry needling for tendinopathy treatment. It seems that tendon needling is minimally invasive, safe, and inexpensive, carries a low risk, and represents a promising area of future research. In further high-quality studies, tendon dry needling should be used as an active intervention and compared with appropriate sham interventions. Studies that compare the different protocols of tendon dry needling are also needed.

Keywords Dry needling · Tendinopathy · Needle tenotomy · Tendon fenestration · Acupuncture

Introduction

The term tendinopathy is a generic descriptor of the clinical conditions characterized by a combination of pain, swelling (diffuse or localized), and impaired performance of tendons and surrounding structures, usually arising from overuse [1]. The terminology is confusing, but generally, the term tendinitis should probably describe a condition that includes an inflammatory process, and term tendinosis referred to a range of clinical findings with histopathology of tendon degeneration.

Although there is a wide range of tendon pathologies, it appears that the majority of overuse tendinopathies in athletes are due to tendinosis [2]. Tendinopathy has multifactorial etiology, but studies examining risk factors of tendinopathy show a lack of uniformity and statistical power [3]. Reliable, well-conducted epidemiological studies are not available for most tendinopathies [4]. Holmes and Lin in their study indicated that there is an increased aggregate association between hypertension, diabetes, obesity, oral contraceptive pills, and hormone replacement therapy and the development of symptomatic tendinopathy [5]. Milgrom et al. found Achilles paratendinitis to be related to training in cold weather [6]. There are many theories about the cause of the tendinopathy, but none of them has solid scientific backing. The mechanical theory of tendon injury suggests that the "overload" of the tendon tissue is the cause of the pathologic process. The

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repetitive trauma from the load in the higher end of the physiologic range may occur within the tendon, especially with repeated and/or prolonged stress. This repetitive microtrauma can lead to matrix and cell changes, altered mechanical properties, and possible symptoms. The vascular theory of tendinopathy suggests that tendons generally have a poor blood supply and are particularly vulnerable to vascular compromise in specific areas [7]. The myofascial theory relates the pathological process to taught and shortened muscles that cause increased traction in the tendon attachment to the bone, or friction between the tendon and its sheath [8]. Furthermore, the myofascial theory also proposes an explanation for many cases of pain around the tendon where there is no local pathological reaction around the tendon. Any tendon and its surrounding tissues can undergo a tendinopathic process, although the common sites of overuse tendon injuries are the Achilles tendon, the patellar tendon, the iliotibial tract, the hamstrings tendons, the rotator cuff tendons, and the wrist extensor and flexor tendons [4].

Microscopically, in the Achilles tendinopathy, the tendon appears with disrupted collagen, a decrease in the amount of type I collagen and an increase in the amount of the weak type III collagen and loss of the classical hierarchical structure. There is also increased ground substance, more tenocytes without their normal fine spindle shape and more rounded nuclei. Vascularity seems increased in tendinopathy, as neovascularization with thick walls, a tortuous appearance, and small lumen ventral from the Achilles tendon and in the paratenon is found in 50 to 88% of symptomatic tendons but not in pain-free tendons. Chronic painful tendons have been shown to exhibit new ingrowth of nerve fibers [9]. The common finding in almost all studies is a lack of inflammation cells.

There are various treatment options for the tendinopathy, but with unproven efficacy. The first line of treatment is medication. If the patient presents with signs of inflammation, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) may be appropriate [10]. In the case of tendinosis, representing a degenerative process, the use of NSAIDs will mainly result in a decrease in pain that does not usually last long after the medication is ceased and actual improvement in the healing process has not been studied [11]. Injections are common treatment modalities in tendinopathies. Corticosteroids are commonly injected in and around chronic tendon injuries, and they frequently provide short-term pain relief but the beneficial effect of corticosteroids on the final outcome remains uncertain since recurrence seems common [11]. Furthermore, steroids are known to have serious local and systemic side effects including numerous reports on the rupture of the Achilles tendon [10]. Transdermal glyceryl trinitrate patches are an alternative therapeutic intervention for a range of tendinopathies. Glyceryl trinitrate has been inferred to reduce pain and inflammation secondary to their nitric oxide–producing action. There are still conflicting reports about the use of this medication, and further evaluation is still recommended [12].

Physical therapy has been commonly used for the treatment of tendinopathies. It comprises various treatment options. A systematic review of the literature suggests eccentric muscle strengthening exercises are a good form of physical therapy while physical therapy modalities such as iontophoresis, ultrasound, phonophoresis, and low-level laser treatment lack sufficient evidence at this time [13]. Musculotendinous strengthening appears to be essential in tendon rehabilitation. Appropriate training increases the diameter and tensile strength of tendons, with tendon fibroblasts increasing the production of collagen type I [14, 15]. The eccentric training program is one that strengthens the muscle-tendon complex while lengthening the complex. There is the greatest degree of evidence for the effectiveness of this treatment in midportion Achilles tendinosis, although it is less effective for insertional Achilles lesions. The effectiveness of soft tissue manual therapy for the Achilles tendon remains unclear [16]. In vitro studies suggest that physical manipulation of tendon cells may affect the cellular output; however, there is little evidence that this occurs in vivo [17, 18]. Extracorporeal shockwave therapy has been advocated for treating a number of soft tissue conditions, including plantar fascialgia, lateral epicondylalgia, calcific and non-calcific tendinosis of the supraspinatus, and tendinopathy of the Achilles tendon. Even so, shockwave therapy remains a controversial treatment option for tendinopathy [19].

Sclerotherapy involves injecting a sclerotic agent into or near a blood vessel, in an aim to degrade the tendinopathy pain generators, namely the abnormal vessels and sensory nerves within the tendinopathic tissue. Some limited evidence suggests that sclerotherapy may be beneficial in those with patellar or Achilles tendinopathies, lateral epicondylalgia, and shoulder impingement [20].

If the tendinopathy does not respond to the conservative treatment options, then more invasive measures are typically considered. Surgery is often considered the last option in the treatment of tendinopathy that persists after exhausting all non-operative options. The most commonly described procedure is open surgical debridement of the involved tendon or peritendinous tissue with repair or augmentation of the tendon as needed. Although good results can be obtained with debridement and/or decompression of chronic tendinopathies, the failure rates can be as high as 20 to 30% with some of these procedures [19].

A procedure done in the past by orthopedic surgeons for Achilles tendinopathy included performing multiple small stab wounds in the tendon [21]. The rationale behind this was to create an inflammatory response that would lead to recovery. This idea is common to a group of treatments known

as prolotherapy where various stimulants are injected to or around tendons or ligaments (including hypertonic glucose and platelet-rich plasma—PRP). One of the theories behind the needling of muscles is that it creates an inflammatory reaction in the muscle.

Dry needling, when used by physicians and physical therapists, is a relatively new treatment modality [22]. It classically refers to needling muscles. Tendon dry needling (percutaneous needle tenotomy) involves repeatedly fenestration of the affected tendon, which is thought to disrupt the chronic degenerative process and encourage localized bleeding and fibroblastic proliferation. This procedure has also been called dry needling to emphasize that the procedure does not involve the injection of any substance, and therefore, placing the needle into the tendon may be the primary reason that the tendon improves and not a specific substance used in prolotherapy and autologous whole-blood for example [23].

The aim of the present paper was to review the use of tendon dry needling as a treatment modality for tendinopathy.

Results

Systematic Reviews

Krey et al. in their systematic review of 4 randomized controlled trials (RCTs) of tendon needling for treatment of tendinopathy state that there is benefit from tendon needling for tendinosis in regard to patient-reported outcomes. Although there is a trend toward improvement with the addition of autologous blood products, it was hard to conclude which technique was superior [24•].

Tsikopoulos et al. compared the clinical impact of platelet-rich plasma (PRP) with placebo injections or dry needling for tendinopathy. In a meta-analysis including 5 RCTs, they conclude that PRP injections did not provide significantly greater clinical relief compared with placebo or dry needling for the treatment of tendinopathy at a 6-month follow-up [25•]. It is important to point out that a placebo group in the studies of Kesiknurun et al. and Krogh et al. included needling and injection of saline solution [26, 27].

Another systematic review assessed the percutaneous needle tenotomy for the treatment of lateral epicondylalgia [28]. It was concluded that percutaneous tenotomy presents an equal and safer alternative to the surgical release of the common extensor tendon for the treatment of chronic tendinosis at the lateral epicondyle of the elbow. However, the studies included in this review were of low research quality—four of the six studies included were retrospective, one prospective cohort study, and only one RCT.

Randomized Control Trials

Most of the studies explore the effectiveness of treatment in lateral epicondylalgia (tennis elbow, a misnomer: lateral epicondylitis), rotator cuff tendinopathy, patellar tendinopathy, and greater trochanteric pain syndrome.

Tennis Elbow

Mishra et al. in a multicenter double-blind RCT with 230 participants evaluated the clinical value of tendon needling with PRP in patients with chronic tennis elbow compared with an active control group injected with 2 to 3 mL of bupivacaine only [29•]. The technique consisted of five penetrations of the tendon and injection of a substance, without ultrasound guidance. Ninety-four patients were enrolled under a 12-week protocol, and 136 patients were enrolled under a 24-week protocol, and data was analyzed regarding 192 patients after 12 weeks and 119 patients after 24 weeks. Successful treatment was set at a > 25% improvement on a visual analog scale (VAS 0–100 scale). There was a statistically significant change in both groups from baseline in the primary outcome measures. Significant differences were not found between groups at 12 weeks, but at 24 weeks clinically meaningful improvements were found in patients treated with leukocyte-enriched PRP. There were no differences in success rates across the centers. The control group in this study was not proper dry needling on account of injection of bupivacaine in the tendon; however, it is usual to use a rapid-onset local anesthetic to anesthetize the skin, subcutaneous tissue, and tendon and there was no use of steroid injection or other active substance. The authors reported about 5 significant adverse events, two of them probably related to the treatment—severe pain (1 for 2 days, 1 for 4 days) in the group of PRP.

In a small RCT with 28 participants, Stenhouse et al. evaluated whether autologous conditioned plasma (ACP) offers any therapeutic advantage over ultrasound-guided dry needling as a stand-alone procedure in the treatment of refractory lateral epicondylitis [30]. Dry needling consisted of passing a 23-gauge needle in and out through the long axis of the tendon without exiting the skin approximately 40–50 times for about 2 min. In the ACP group, 2 mL ACP was injected in addition to dry needling. The procedure was again repeated at 1 month. Ultrasound was used for diagnosing the tendinopathy and for guidance during the procedure, but not as an outcome measure. VAS (0–10) and Nirschl scores were recorded prior to the first procedure, at 2 months and at the final follow-up of 6 months. Treatment was successful in both groups at 6 months with a 34% reduction of VAS in the dry needling group and a 48.5% reduction of VAS in the ACP group. The authors conclude that there is a trend toward greater clinical improvement in the short term for patients treated with additional ACP; however, no significant difference between the

two treatment groups was demonstrated at each follow-up interval. No adverse events were reported during the trial, but three participants exited the trial prior to the second treatment due to increasing elbow pain (two within the ACP group and one within the dry needling group). The limitations of the study were the small sample size and lack of power analysis.

The recent RCT of Uygur et al. compared the outcomes of dry needling and first-line treatment consisting of ibuprofen 100 mg twice a day and a proximal forearm brace [31•]. In total, 92 patients completed the study. The patients were diagnosed with lateral "epicondylitis" according to physical examination and x-rays of the elbow to rule out radio-humeral joint arthritis, osteochondritis dissecans, or osteonecrosis. No sonographic examination was used. In the dry needling group, five 0.25 × 25-mm stainless steel acupuncture needles were inserted in the most painful areas at the lateral epicondyle. The needles were directed through the skin and fascia to the bone (3–5 mm) and were rotated three to four times and left in place for 10 min. Applications were repeated twice per week for a total of five sessions. In both groups, significant differences were detected at the 3 week follow-up. The control group showed no effect at the 6-month follow-up, whereas dry needling was effective at both 3 weeks and 6 months. Two patients in the dry needling group could not tolerate the intervention, and one had a local hemorrhage. Although this study had a sample size calculation, one-fourth of the patients in the control group had to be excluded from the study because they used other treatment methods and the analysis was not by "intention-to-treat." The authors concluded that dry needling is a safe and effective treatment method for lateral "epicondylitis."

Rotator Cuff Tendinopathy

The effects of tendon needling in 30 patients with rotator cuff disease were studied by Rha et al. in a prospective double-blind RCT [32•]. Authors compared the effects of tendon needling, with or without injection of PRP. The main outcome measurement was the Shoulder Pain and Disability Index, and all patients had sonographic examinations before and 6 months after the treatment. The technique of dry needling used was similar to that in the study of Stenhouse—passing a 25-gauge needle through the lesion of the tendon approximately 40–50 times under ultrasound guidance. PRP injections and dry needling were performed twice with a 4-week interval between injections. Both groups demonstrated significant clinical improvements. PRP injections provided more symptomatic relief and functional improvement than dry needling at a 6-month follow-up. The improvement in the range of motion of the shoulder was not different between the PRP and dry needling groups. There were no serious adverse events attributable to the treatment. The study did not have a sample size calculation/power analysis.

Achilles Tendinopathy

Bell et al. in a prospective double-blind RCT with 50 participants assessed the effectiveness of peritendinous autologous blood injections in patients with mid-portion Achilles tendinopathy [33•]. Both groups underwent a standardized 12-week eccentric calf strengthening program in addition to two peritendinous needling procedures 1 month apart, with or without the use of autologous blood. The primary outcome measure was the Victorian Institute of Sports Assessment-Achilles (VISA-A) score. Ultrasound was used to confirm the diagnosis, but it was not used to guide needling or as an outcome measure. In both groups, the needle was firstly inserted perpendicular to the tendon, with a second pass aimed at 20° superiorly in the plane of the tendon, and a third pass aimed 20° inferiorly. In the treatment group, patients received 3 mL of blood injected during the three passes. Both groups showed clinically meaningful improvement in the mean VISA-A scores by 6 months, and there was no significant difference between groups. No adverse events were reported. Sample size calculation and power analysis were performed, using the "intention-to-treat" principle.

Patellar Tendinopathy

Dragoo et al. used a prospective double-blind design to evaluate tendon needling with or without the addition of PRP in patellar tendinopathy [34•]. A total of 23 patients who had failed nonoperative treatment (persistence of symptoms after 6 weeks (12 sessions) of physical therapy with eccentric exercise) were included. The diagnosis was made by clinical examination and was confirmed by MRI (enhanced signal intensity in the proximal patellar tendon, increased tendon size in the anteroposterior direction, and poor definition of the posterior tendon border). Both groups underwent ultrasound-guided tendon penetration 10 times with or without the addition of PRP. All patients were instructed to follow a standardized program of eccentric exercises. The primary patient-reported outcome was VISA scores. The VISA scores improved significantly in the PRP group over time, and the PRP group had improved significantly more than the dry needling group at 12 weeks, although both groups showed statistically significant improvement and the difference between groups disappeared at 26 weeks. No adverse events were reported. The sample size calculation was performed, and the data were analyzed using the "intention-to-treat" principle. The limitation of this study is the younger age of the PRP group which could potentially bias the results.

Greater Trochanteric Pain Syndrome

Jacobson et al. in the single-blinded prospective study compared ultrasound-guided percutaneous tendon dry needling to

PRP injection for the treatment of greater trochanteric pain syndrome [35]. A total of 30 patients with the presence of gluteus minimus or medius tendinosis or a partial-thickness tendon tear were included. Ultrasound examinations of the hip were performed to evaluate for a gluteal tendon abnormality and to exclude other types of hip disorders. The patient had failed conservative management, including physical therapy and nonsteroidal anti-inflammatory drugs. In the tendon dry needling group, the 20-gauge needle was passed approximately 20 to 30 times at various angles through the abnormal tendon. In the PRP group, the needle was inserted into the deepest aspect of the tendon abnormality, and the PRP was injected; the number of times the needle was passed through the tendon was less than 10. The patient care after treatment was not controlled. Pain scores were assessed after 1 and 2 weeks approximately. Both groups showed improvement in pain scores at 1 and 2 weeks, with no significant difference between the treatments. The study did not have sample size calculation and there was only a short-term follow-up. However, the authors did a limited retrospective follow-up at an average of 92 days with no significant difference between the treatment groups ($P = .0815$).

Cohort Studies

Housner et al. in a prospective cohort study in 2009 reported the results of sonographically guided percutaneous tenotomy using a 22-gauge needle in 14 tendons including 5 patellar, 4 Achilles, one proximal gluteus medius, proximal iliotibial tract, proximal hamstring, common extensor elbow, and proximal rectus femoris [36]. All patients had failed to respond to conservative treatment. Approximately 20 to 30 needle passes were made through the sonographically abnormal region of the tendon. During each procedure, approximately 3 to 6 mL of the lidocaine-bupivacaine mixture was injected into the tendon for anesthesia. They showed a statistically significant reduction in mean pain scores 4 weeks after the procedure, which was maintained at the 12-week follow-up. No complications were noted.

In another study in 2010, Housner et al. retrospectively evaluated the results of using ultrasound-guided tendon dry needling for the treatment of recalcitrant patellar tendinopathy [37]. The study included 32 patients (47 patellar tendons). The methods were similar to their prospective study from 2009 [36]. At an average follow-up of 45 months, 72% were able to return to sports and 81% reported excellent or good overall satisfaction scores. Kanaan et al. in 2013, using the patient data from the previous study of Housner, compared pre-procedure sonographic findings to a change in the functional pain score after dry needling of the patellar tendon [38]. They found that the presence of a well-defined area of tendinosis of the patellar tendon correlated significantly with clinical improvement of patients after sonographically guided patellar tendon dry needling [34•].

McShane et al. in two retrospective studies report their experience with sonographically guided dry needling in patients with chronic tendinosis of the common extensor tendon of the lateral epicondyle, while in the first study from 2006 they added a corticosteroid injection and in the second from 2008, they used the same technique of tendon dry needling, without the steroid injection [39, 40]. The technique of the dry needling in the studies was similar—a 20- or 18-gauge needle was passed repeatedly parallel to the longitudinal plane of the tendon. After the procedure, patients were instructed to perform passive stretches and to have physical therapy.

In the first study from 2006 with steroid injection, the average follow-up time was 28 months. 63.6% of participants reported excellent outcomes, and 16.4% good. No adverse events were reported in any patients [39].

In the second study from 2008, the authors reported a similar outcome at an average follow-up of 22 months—57.7% of the respondents reported excellent outcomes, and 34.6% good. They concluded that sonographically guided tendon dry needling for lateral elbow tendinosis is safe and effective, and subsequent corticosteroid injection is not necessary [40].

Jacobson et al. in a retrospective study in 2015 evaluated the effectiveness of ultrasound-guided tendon dry needling about the hip or pelvis [41]. The study included 22 tendon fenestrations—11 gluteus medius, 2 gluteus minimus, 8 hamstrings, and 1 tensor fascia lata. The needle orientation was either long axis or short axis to the tendon and passed 20 to 40 times. The average interval to clinical follow-up was 70 days. They report a marked improvement in 45.5% and some improvement in 36.4% of patients.

Discussion

Tendon dry needling as the standalone procedure is used in the common sites of tendinopathy including wrist common extensor origin, patellar tendon, Achilles tendon, rotator cuff, gluteus medius and minimus, hamstrings, rectus femoris, and tensor fascia lata. There is significant heterogeneity of techniques. Most of the authors described that the needling consisted of passing a needle (20 to 23 gauge) in and out through the tendon about 20 to 50 times [30, 32•, 35–37, 41]. Mishra et al. suggested only 5 penetrations of the extensor carpi radialis brevis tendon, Bell et al. only 3 penetrations of Achilles tendon, and Dragoo et al. performed 10 ultrasound-guided penetration of patellar tendon [29•, 33•, 34•]. The number of needle passes may vary based on factors, such as patient characteristics, severity, and size of the tendinopathic area, presence or absence of tears, operator experience, and comfort level, and needle gauge used [42]. Uygur et al. used a slightly different method with five 0.25 ×

25 mm stainless steel acupuncture needles in the most painful areas at the lateral epicondyle [31]. The needling procedure was performed by a physician in all studies, except the study of Uygur et al. where the intervention was performed by a physical therapist.

In the RCTs reviewed in this paper, the dry needling was studied as a control group and compared with dry needling with another intervention. Only the study of Uygur et al. compared the outcomes of dry needling and first-line treatment, where the control group did not undergo needling [31]. All RCTs lacked a true control group in which no intervention was done, although the "watchful waiting" control group would be useful, as the natural history of tendinopathies is usually self-limited. Most authors explained not having a no-treatment group as related to ethical considerations: as there is evidence the treatment (injections) works, it would have been unethical to include a true control group. There were probably concerns about the placebo effect and the ability to recruit patients to a no-treatment group. In most of the studies, the patients had to fail conservative management in order to be included. The timing of the intervention varies widely from 6 weeks to 6 months in the RCTs, and up to 60 months and 105 months in the retrospective studies [30, 32•, 34•, 40, 41].

The systematic reviews of tendon needling for treatment of tendinopathy state that there is benefit from tendon needling for tendinosis in regard to patient-reported outcomes [24•, 25•, 28]. Most of the RCTs also support the effectiveness of tendon needling. The PRP injections did not provide significantly greater clinical relief compared with placebo or dry needling for the treatment of tendinopathy. The percutaneous tenotomy presents an alternative to the surgical release of the common extensor tendon for the treatment of chronic tendinosis at the lateral epicondyle of the elbow [24•, 25•, 28].

The outcome measures included patient-reported symptom scores and objective findings. There was a statistically significant improvement in the patient-reported symptom scores in most of the studies [29•, 30, 31•, 32•, 33•, 34•, 35]. Rha et al. reported about an objective improvement looked at an ultrasound evaluation [32•]. Uygur et al. did not examine all the patients with ultrasound, although the sonographic images of a few patients indicated that radiological recovery of the tendon is possible [31•].

The studies were inconsistent about the therapy used after the procedure. Most of them allowed exercises, but they were not structured and were without proper post-intervention protocol. Bell et al. instructed the patients to use a standardized eccentric training program, while Dragoo et al. used the standardized 5-phase program of eccentric exercises, which was provided directly to their physical therapists [33•, 34•].

The outcome measures included patient-reported symptom scores. Rha et al. looked at an ultrasound evaluation, which was done at 6 months after needling and reported objective improvement [32•]. Uygur et al. examine some of the patients with ultrasound and report that radiological recovery of the tendon is possible after dry needling [31•].

Only two studies reported complications. Mishra et al. reported 5 significant adverse events, two of them (severe pain) probably related to the treatment [29•]. Uygur et al. reported one patient with local hemorrhage and two patients that could not tolerate the pain during the intervention [31•].

The overall conclusion regarding adverse events is that tendon dry needling is a safe treatment method.

Conclusions

Current research provides initial support for the use of tendon dry needling as a stand-alone procedure for tendinopathy. It seems that it is a safe and effective treatment method, although there is a vast diversity regarding the technique of the needling, ultrasound guidance, and additional treatments used.

The different methods of dry needling can cause some confusion in the use of the term. Most of the studies in the field of tendon needling were made about the fenestration technique, which is usually limited to physicians. Although Uygur et al. demonstrate the effectiveness of the technique of dry needling using acupuncture needles and without ultrasound guidance, provided by a physical therapist as first-line treatment [31•]. Tendon dry needling with acupuncture needles is minimally invasive and inexpensive, carries a low risk, and represents an interesting area of future research and clinical use.

Future investigations are needed to provide high-quality evidence for the effect of tendon needling on tendinopathy. Tendon dry needling should be used as an active intervention and compared with an appropriate sham intervention to control the placebo effect. Studies comparing the different tendon dry needling protocols are also needed.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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